ماجستير تناسليه (2)

ANATOMY OF URETHERA
(STDS)

د/هانى ابوالوفا

د. مسلم
just print
01025329200- 0502200362

Anatomy of Urethra

♂ Urethra

def : Canal that Extend from Bladder Neck to Ext. urethral Meatus passing Through substances of Corpus Spongiosum.

Length : 20 cm.

shape : "S" shaped

Q : Why predisposed to chronic Inf. ? urethritis.

d.t. 2 factors < always Closed & open only during Micturition
S-shaped

Anatomy

- Ant. urethra — 15 cm.
  - Bulbous urethra
  - penile or pendulous urethra
- Post urethra — 5 cm.
  - prostatic urethra
  - Membranous urethra

** Post urethra (5cm = 3+2)

Prostatic urethra

From neck of bladder to neck of prostate (passing through substance of Prostate)

- length 3 Cm
- Ch
  - Widest part
  - Most distensable part
  - has elevation on its post wall called "Verumentanum or "Colliculus seminalis"

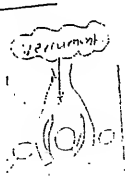
Membranous urethra

- Extend from Neck of prostate passing through Ext. urethral Sphincter enclosed in Urogenital diaphragm.
- length 2 Cm.
- Ch
  - Thickest part
  - Narrow
  - Muscular organ (Sk m + Smooth m)
- lined by Col. Epithelium

** Related to 3 openings:

* opening of prostatic utricle (remnant of Mullerian duct) → open on Top of C. Seminalis (it's a blind pouch)
  - Lined by "Transitional Epithelium

* 2 openings of Ejaculatory ducts (Slit like) on Both Sides of Colliculus → "C. Seminalis



* 20 openings of prostatic ducts on either Side of Verumentanum by Depression (Fossa) called "prostatic Sinus"

** Ant. urethra

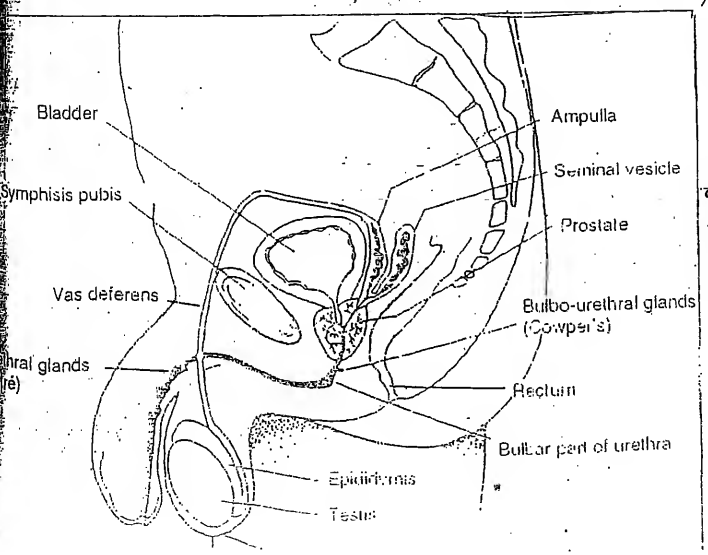
- 15 Cm
- Extend From membranous uretha tipp the end of Ext. urethral
- All lind by Columnar epith. Except Fossa Navicular (St. Sq. non Keratini zed).
- 2 parts

Bulbous urethra

- Surr. BY bulb of penis & bulbospongiosus Muscle.

Penile = pendulous = Spongy urethra

- start as continuation of bulbous urethra at lowest level of SP. (S. pubis).
- ends by passing Through glans penis to Form dilatation (fossa Navicularis) - end of Ext. Meatus (Narrow Part).



Glands Related to the Urethra

- gland
- ducts
- secretion

Cowper's (Bulbo-urethral glands)

- present at both sides of Memb urethra &
- Their ducts open into bulbar urethra
- (E) → Prosemen on Excitation

Littré's (Urethral or Periurethral glands)

- Multiple glands present on submucosa of penile urethra
- open by Multiple ducts on the Roof & sides of Penile urethra
- Openings of the ducts Found on depressions called « Lacuna of Morgagni »

Tyson's

- proximal to Coronal Sulcus
- ducts: open on either side of Frenulum (Fold on under surface of glans penis
- Secrete: sebaceous secretion (Smegma) to help retract prepuce over the glans (in non-circumcised)

- Paraurethral ducts
  - Small blind Channels that run parallel to terminal Part of urethra & open near Ext. Meatus

Mucosal Folds of Morgagni

- Largest one is Near the Fossa Navicularis & called « Lacuna Magna » on roof of urethra

Fossa

Smegma
Accumulation under Prepuce → irritation → SCC of penis

When Introducing Catheter:
- To avoid Impaction in lacuna of Morgagni

Sphincters of the Urethra

Internal Sphincter

- Ejaculation, Urination
- Control the Bladder
- "Neck & prostatic urethra above openings of Ejac. ducts.
- Involuntary non striated
- (So supplied by autonomic).

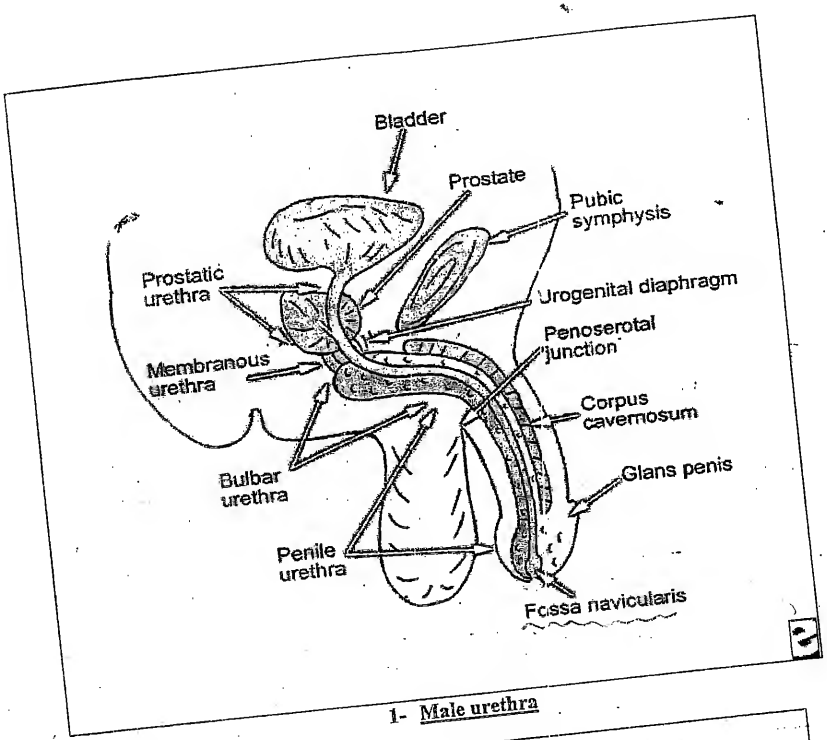
Ext. sphincter

- Control the membranous urethra
- Composed of Striated mu.
- (So supplied by somatic)
- (Pudendal N.)

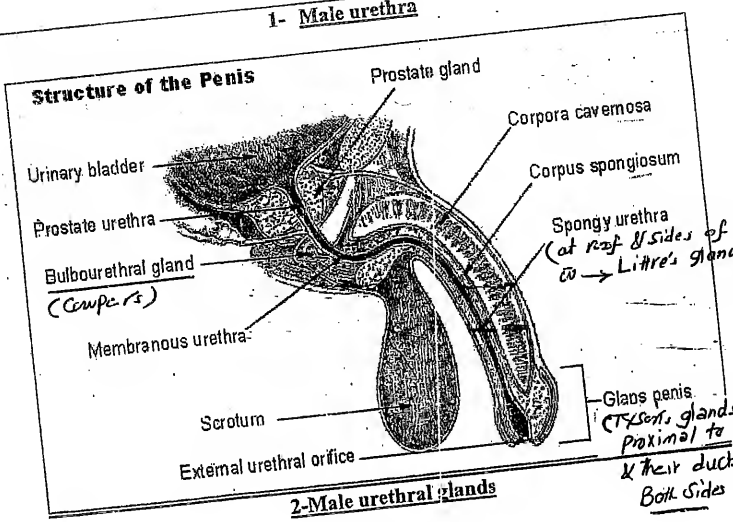
Clinically important point: *Failure of the prostatic utricle to regress during embryological development may encroach on the surrounding ejaculatory ducts leading to their obstruction and infertility.* (EDO).

Female urethra

- 4cm
- Extend from UB to Ext. urethral Meatus
- Epith. → Proximal: Transitional
  → distal: st. sq. Epith.
- Glands → ① Skenes: Near lower End of urethra & open into urethral Meatus.
  ② Bartholins: → Pair of gland.
  - present at post. ⅓ of Labia Majora
  - open at inner surface of Labia Minora.
  - at ant. wall of Vagina around lower end of urethra & drain into it.
  ③ Small urethral glands (Similar Lmfre



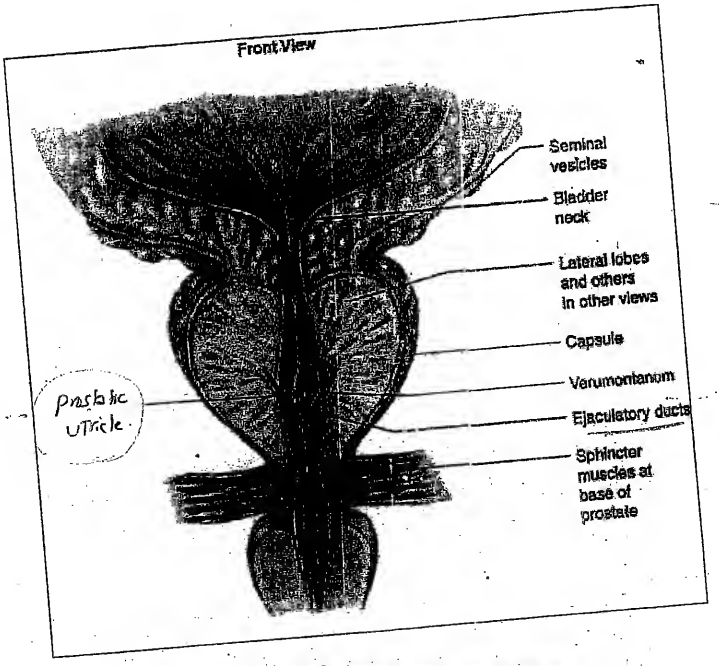
1- Male urethra

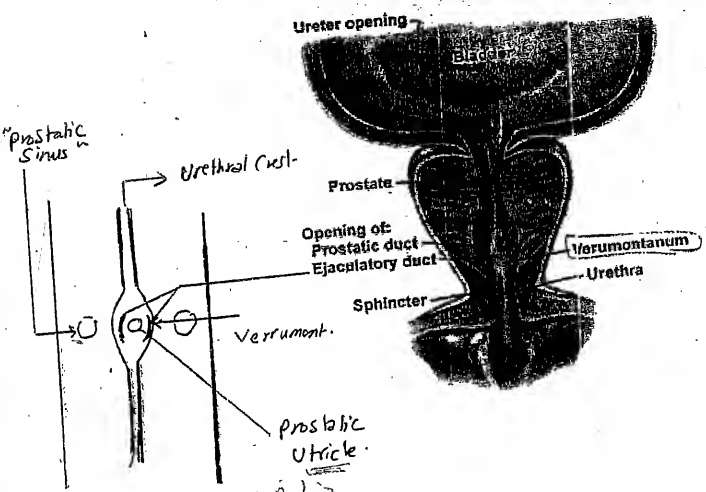


2-Male urethral glands

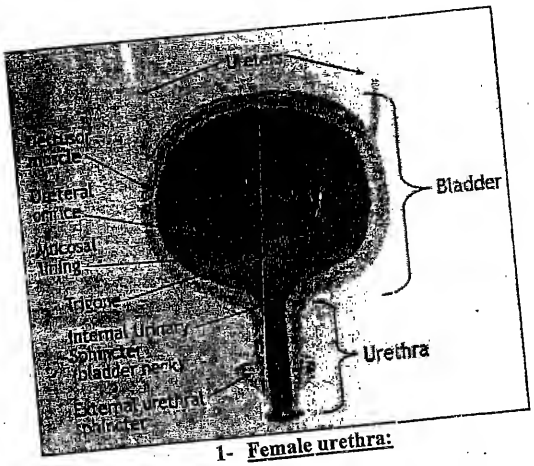
(Tyson's glands present proximal to sulcus & their ducts open on both sides of Frenulum)

dorsal aspect of penis

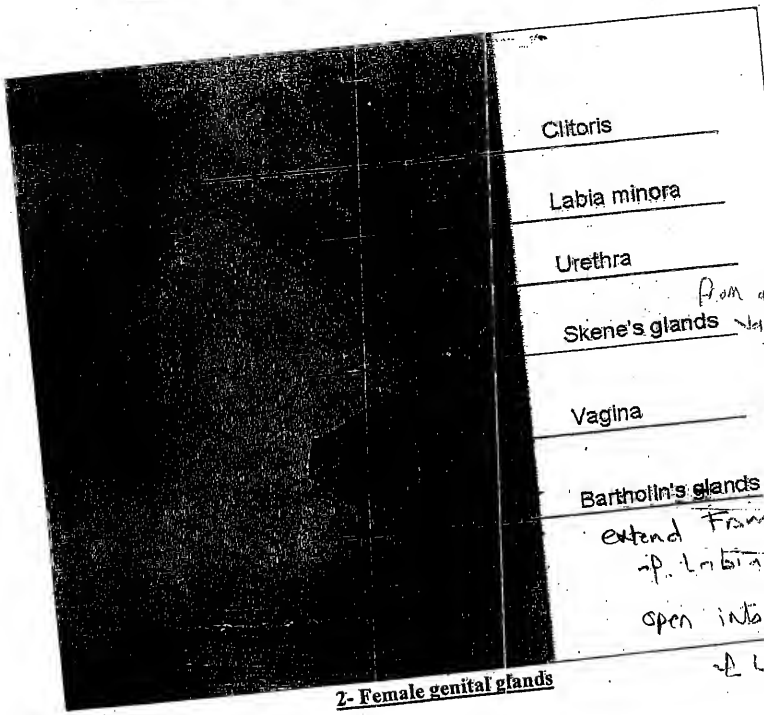




colliculum Seminalis



1- **Female urethra:**



2- **Female genital glands**

Gonorrhea (2011)

Def. Acute Infectious dis. of Genitourinary MM caused by N.G

Almost exclusively Transmitted Sexually.

Biology of NG

(N.Gal)
1- Microbiology
2- Structure & Virulence
3- Antibiotic Resist.
4- Pathogenesis

A- Microbiological characters:

- G-ve, 0.5-1 µm. Diplococci
- Aerobic or facultative anaerobe (Can grow in presence of air or Vari Low (2) Tension)
- Kidney shapped diplococci
- Multiplicate in Intracellular (inside PMNL & epith. cells) [NG: Intracellular in acute inf.; extracellular: in Chronic & Very early acute]
- None Motile, Non capsulated, Non-Sporulated
- Can't survive for long time outside the body rapidly destroyed BY: Dryness, Heat, antiseptic, Saliva (Contain Amino-glycosides)
- Can resist: Dryness, antiseptic

B- Structure and realted function:

1. Cell (plasma) membrane (CPM) → permeability
2. Peptidoglycan layer → Strength & osmotic equilibrium.
3. outer Membrane: (Envelope) (OM)

(i) Lipopolysaccharides
- endotoxin, ch. BY:
- Structural integrity of NG. (protect ogamst chemical damage)
- Induct of Immunological Response.

(ii) Lipoproteins
↓
Link bet. Pephido-glycan & OM.

(iii) OPa-Protein = opacity associated (OPa.)
↓
- Adherence to Phagocyteo & epithelicim.
- Invasion.
- Resistance, evasion from Immune System by:
  - down-regulat- of Immune Cells
  - Antigenic Variat-
- So reinfect- is possible

(iv) Porins (PorA & B)
Pores or Channels in OM play a role in Virulence.
- PorA NG has inherent resistance to Igs & Ability to invad the epith (explain their role in Bacteremia)

For chemical Molecules.

& adhesion

Periplasmic space: Space bet. Peptidoglycan & both PM < OM

Pili (Fimbriae): (grasping - Hooks)
- Attachment to epith.
- resistence against Neutrophils.

- Virulence factors:
1. Opa protein
2. porins
3. pili
4. Lipo poly saccharides (endotoxins) → DGI
5. Produce IgA-protease.

Mechanism of Antibiotic Resistance:
(1) see later (25:2)

(2) 2- L-form of NG: Alleratⁿ in its Morphology (Failed cell wall synth) may occur spontaneously or by repeated Culture → its insensitive to penicillin only

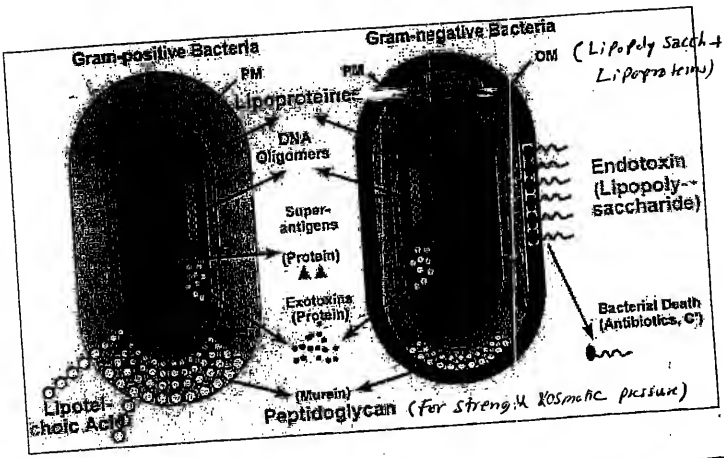
D. Pathogenesis: The organism has predilect^n to Columnar or Cuboidal epithelium so it attacks:
- In Male: Epididymis, SV, prostate, Cowper's & Littrés
- In Female: Endocervix, F.Ts, Skene's & Bartholin glands.
- In Male & female: Urethra, rectum, oropharynx & Conjunctiva

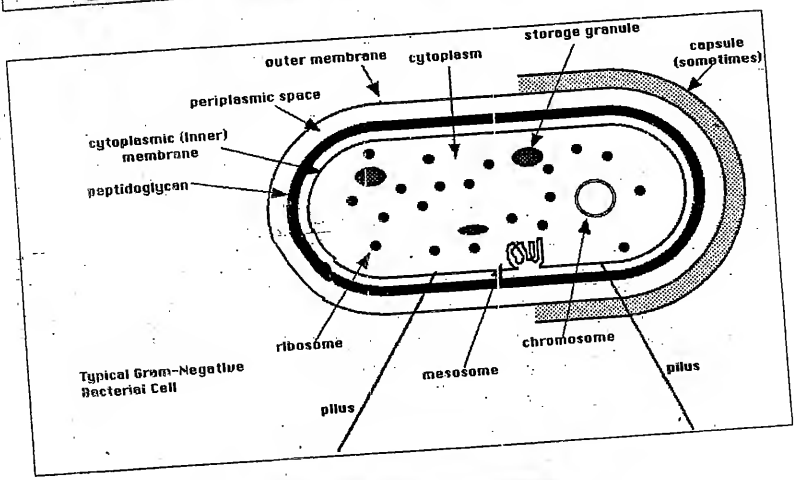
(except Trigm)
UT
Na
ma

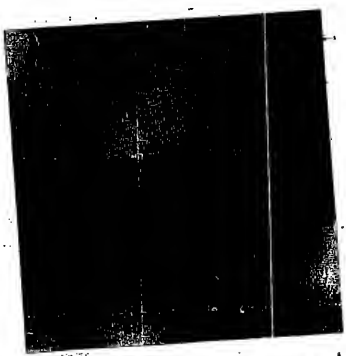
Gonococci attach to the host mucosal cell (pili and Opa proteins play major roles) and, within 24-48 hours, penetrate through and between cells into the subepithelial space. A typical host response is characterized by invasion with neutrophils, followed by epithelial sloughing, formation of (submucosal) microabscesses, and purulent discharge. If left untreated, (macrophage and lymphocyte) infiltration replaces the neutrophils. Some gonococcal strains cause an (asymptomatic) infection, leading to an asymptomatic (carrier) state in persons of either sex. The ability to grow (anaerobically) allows gonococci, when mixed with (refluxed menstrual blood) or attachment to (sperm), to secondarily invade lower genital structures (vagina and cervix) and progress to upper genital organs (endometrium, salpinx, ovaries).

Epidemiology

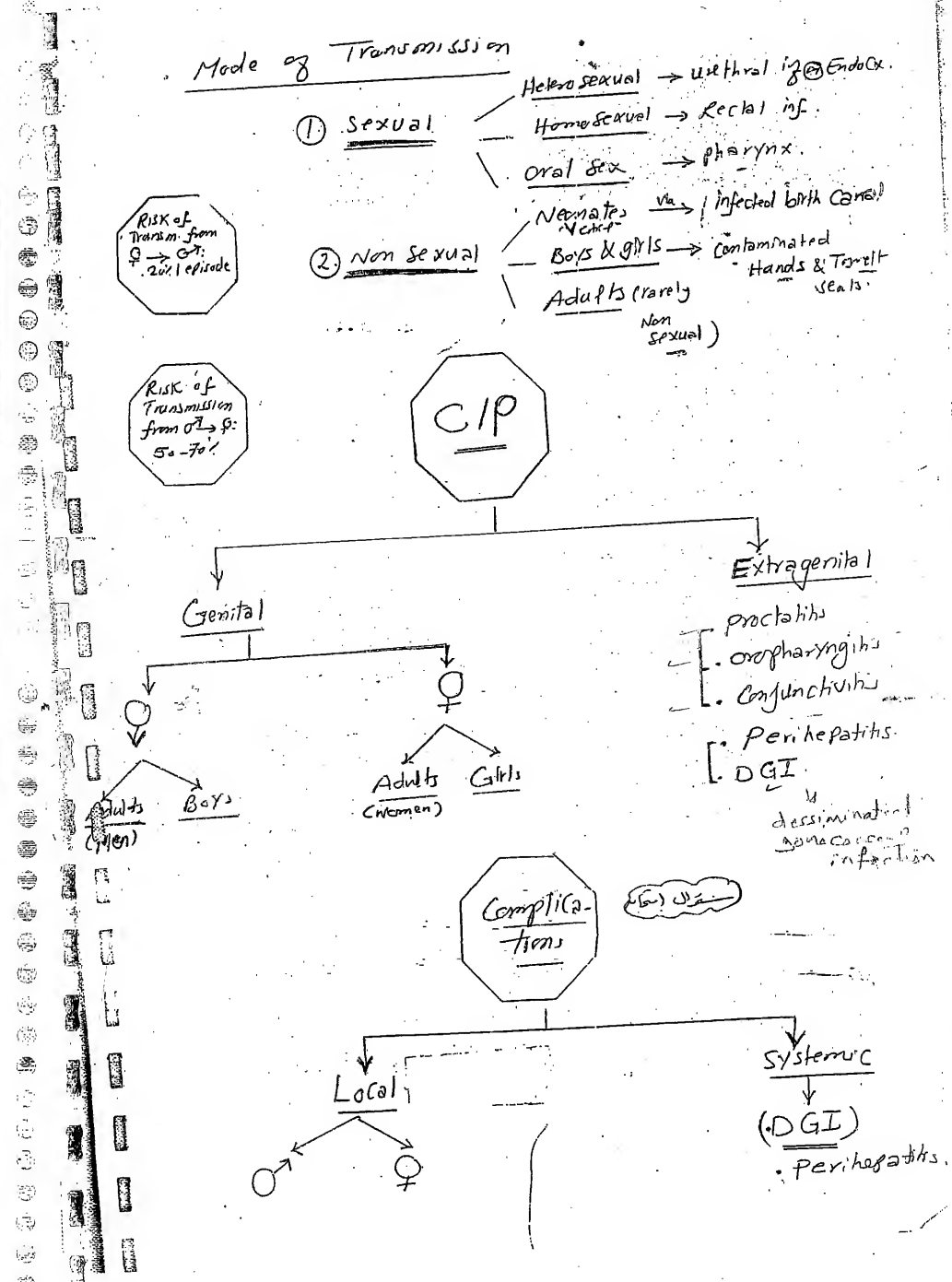
- Incid: 200 millions/y.
- Age: Usually Adolescent & Young Adults (20-40)
  - ± Children < usually: Sign of Sexual Abuse
    May be: non Sexual transmission bet. Children & From Adults To Children or Infected Towel. From
- M/F (1.5:1)







Stained smear : Streptococci
Diplococci


Mode of Transmission
1. Sexual
Hetero sexual → urethral inf @ Endocx.
Homo sexual → Rectal inf.
Oral sex → pharynx.
2. Non Sexual
Neonates via infected birth canal
Boys & girls → contaminated Hands & Toilet seats.
Adults (rarely Non sexual)
Risk of Transm. from ♀ → ♂: 20% / episode
Risk of Transmission from ♂ → ♀: 50-70%
CIP
Genital
Extragenital
Proctalitis
Oropharyngitis
Conjunctivitis
Perihepatitis
DGI
disseminated gonococcal infection
Adults (Men)
Boys
Adults (Women)
Girls
Complications
Local
Systemic
(DGI)
Perihepatitis.

Adult Male CIP (Gonococcal urethritis)

- IP: 2-7 ds (usually 5)
- CIP < 15% → Asymptomatic → Carrier
  < 85% → Symptomatic:

→ FAHM (±)

- Manifs of Ant. urethritis (Early)
  - Dysuria
  - Discharge
    - Profuse
    - purulent
    - Yellowish-greenish
    - stains underclothes
    - ± scanty & Mucoid (as NGU)

- Manifs of post urethritis (Late & Un-Treated) (12-14 ds)
  - Ant. urethritis manifs
  - Frequency
  - Urgency
  - Hematuria (± priapism)

- Urinary Meatus → red & Edematous (+rigors & Columnar epith)
- L.N. → Enlarged & Tender (Bubo)

Gonorrhea in Adult Women (Gonococcal cervicitis)

- IP: ≥ 2 ws (> Men)
- CIP
  - 50% Asymptomatic
  - 50% Symptomatic

Most often & less common

- Cervicitis (90%) (Endocervicitis)
  - Commonest presentation ✓ back pain
  - Manifestations:
    - Commonest → low backache, discharge from Ext. os ♀ is ... & Eroded
- Urethritis (80%)
  - Dysuria
  - Discharge
  - Frequency
  - Urgency
  - Hematuria
  - Ext. Meatus → red & oedem.
  - L.N

- in ♀:
  - Commonest Sites
  - CX 90%
  - Urethra 80%
  - rectum 40%
  - pharynx 2%

→ ↓ Sub-Secretion & indirate Trigonitis.

NB: A normally looking Vagina & Cervix doesn't Exclude Inf. This because (racemove) Nature of Cervical glands → Chronicity of Infects
é formatn of Bluish Cysts (Nabothian follicles)
d.t Duct obst (d.t creeping of vaginal Epith. over eroded Cx).

Gonorrhea in Boys:

AEt < usually Sexuall assault
may be: Non sexual Contact
in Household.

CIP: dysuria, discharge & proctalitis.
As of t proctalitis rectum

Gonorrhea in Girls:

AEt: as in Boy (rape).

CIP: Vulvo Vaginitis + adult like manifs < dysuria, discharge, proctalitis.

↳ most common presentation

Extra-genital Infects

1. Gono. Conjuctivitis may affect

Adults
.dit autoinoculation
→ (usually unilateral)

Ip: 2-5 ds

Neonates (ophthalmia Neonatorum)

affects the Neonates during Vaginal delivery (Vertical Transmission)
(usually Bilat)

- Ophthalmia Neonatorum (usually Bilat) ↓
  may → Blindness.

CIP (Both): → Purulent Conjunctivitis
- Keratitis.
- Abscess.
- Blindness.

2. **Oropharyngitis**
   - d.t oral Sex
   - mild Pharyngitis. non sp.

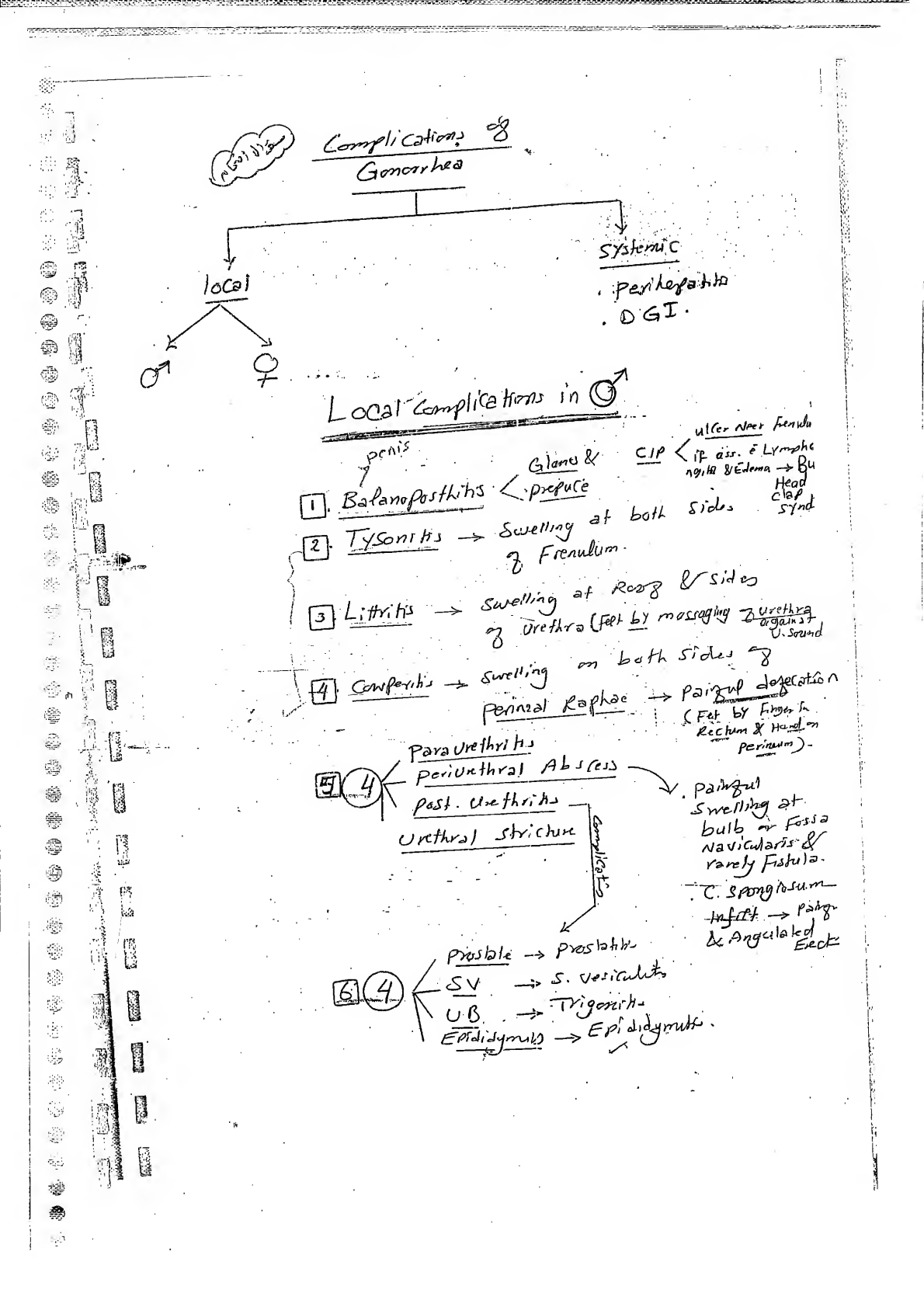
3. **Proctatitis.** (proctitis).

Mode:
- ♂ → Homosexuality
- ♀ → Anal sex or local spread from Gonococcal endocervicitis (Contaminated by endo Cx. discharge) — 50%.

NB: 50% of women c Gonorrhea have proctitis.

DD of proctitis
- Gonorrhea
- Candida
- ♂
- Genital wart
- Chlamydia
- HSV
- non specific.

CIP: ± Asymptomatic or Rectal manifs:
- Pain
- Pruritus
- Tenesmus
- discharge
- Bloody diarrhea.


Complications of Gonorrhea
local
Systemic
. perihepatitis
. DGI.
♂
♀
Local Complications in ♂
penis
1. Balanoposthitis < Glans & prepuce
CIP < ulcer Near frenulu
if ass. ē Lymphe
ngitis & Edema → Bu
Head
clap
synd
2. Tysonitis → Swelling at both sides of Frenulum.
3. Littritis → Swelling at Root & sides of urethra (Felt by massaging urethra against U. Sound
4. Cowperitis → Swelling on both sides of Perineal Raphae → Painful defecation (Felt by Finger in Rectum & Hand on perineum).
5 4
Paraurethritis
Periurethral Abscess
Post. Urethritis
Urethral stricture
Complication
. Painful Swelling at bulb or Fossa Navicularis & rarely Fistula.
. C. spongiosum infect → Painful & Angulated Erect
6 4
Prostate → Prostatitis
SV → S. vesiculitis
UB → Trigonitis
Epididymis → Epididymitis.

Complications of Post Urethritis

1. Prostatitis
2. Seminal vesiculitis
3. Epididymitis

---

1. **Prostatitis** (rare)
   - may be < acut / chr. → usually d.t Non specific inf.
   - occurs as Complication as post. Urethritis
   - C/P:
     - Pain: pelvic, suprapubic, penile.
     - Voiding Symptoms: Dysuria, Frequency, Urgency, Hematuria. + no discharge
     - Sexual Symptoms: ED, PE, priapism & Hemospermia.
     - Infertility ✓
     - Abscess may open in to < Post. Urethra → Perineal pain & relief of S&S
       Rectum → gonococcal proctitis
     - PR Examination ??

2. **Seminal vesiculitis** → عملياً بنقصر فيها خطر القذف
   - As prostatitis +
   - spasmodic pain @ ejac.
   - Morning Gleet. (نزيف) → ↓ Secretion
     ذكر ما يجيش منه

3. **Epididymitis** see infertility.

Local Complications in ♀

Painful tender swelling at base of L. Labia Majora
- difficult sitting & walking

- Skenitis: with Paraurethral Cyst or Abscess
- Bartholinitis: with Bartholine Cyst or Abscess

Chr. pain
Infertility
Ectopic preg.
Neoplasia

Up. GIT ← (25%): PID: Salpingitis & Pyosalpinx
- Parametritis: endometritis
- Pelvic abscess
- Peritonitis
- Proctitis: → ± Asympt. anorectal manifs.
- Tubal Obst
- Tubo-ovarian abscess.

↓ common local complicat

Systemic Complications

A. Perihepatitis... → spread of inf. to peritoneum

(Fitz Hugh-Curtis Synd)

AEt: spread of inf. By: In. ♂ & ♀ → Blood
In ♀ only → Through the Tubes & their continuation to the peritoneum.

Violin-String Complicat (adhesion bet liver & diaphragm).

CIP: (1) Acute onset of:
- Fever
- Nusea
- Pain → Rt Hypochondriac ↑ by cough → referred to shoulder

(2) Complications ✓

B — Disseminated Gonococcal Infection (DGI)

Gono-Coccemia
Arthritis – Dermatosis Synd.

- Incid: 0.5–1% (d.t Blood spread → Capnary embolization by cocci & release of Toxins)
- Risk factors:
  1. Menestruation & pregnancy (d.t changed PH → Bacgn ↑ Cervical shedding ↓ Bact. enzs in Mucosa ♀ Ca; anH)
  2. Hypo Complement-emia (C5, 6, 7 & (8)).
  3. AUH type of organism.
  4. Resistance To bactericidal IgM (d.t Antigenic Variation in Their Poly Saccharide Endotoxins).
  6. pharyngeal inf.

Antipilus Antibody

High incid of Asympt. ♀ → ⑤ → onset of dissemination

CIP : 2 forms:

Mild form

Fever (< 39.4°C)

Arthritis

- Polyarthralgia
- Tenderness
- Limitation
- Erythema
- ± purulent

→ Large joints

Rash

- Maculopapular, Vesicular, Bullous Pustular, Hgic or Necrotic
- Usually at distal Extremities e.g. (Palm, Sole & Arm, Jaw)
- Spare: Face, scalp & mouth.

Severe form

- Hepatitis →
- Cardiitis → Tach. & Murm
- Encephalitis → meningism
- Osteomyelitis.
- Myositis → ss abscess
- Teno Synovitis → of hand
- Iridocyclitis. (Allergic re

NB Eye affects: Conjunctivitis, Iridocyclitis

Diagnosis → إزاي؟ (مش دلوقتي)

1. Glass Tests
2. Stained smear.
3. Culture & Sensitivity.
4. Biochemical Reactions.
5. Antigen detection.
6. Gene detection.
7. Others

1. Urine analysis & Glass Tests:

2 glass Test

- Micturate in 2 glasses:

If there is:
- Ant. urethritis:
  - 1st. specimen → Heazy
  - 2nd " → clear
- Post urethritis: 2 glasses or specimens are Hazy.

3 glass Test.

3 glasses: contain.

- 1st → Irrigated ant urethra.
- 2nd → contain the (few) amount passed by urinat
- 3rd → remainder of urine passed by urinat

↓ If:

Turbidity in:
- 1st glass → ant urethr
- 2nd " → Post
- 3rd " → Trig (Blad Inf

2 Stained Smear: the sample used ± : urine / discharge / swab.

(A) Urine :- بناخد اول سرايول. بشرط انه يكون بول
مش فترة بيتسم انيتا فيه اكل ماكرم سرايزر
If exam → if ≥ 10 PMNL/HPF → Urethritis.

(B) Exudate: Taken by swab →
- Women: → endo Cx & urethra.
- MEn: → urethral swab or Bacteriologic loope.
- Rectal inf.: → under anoscopy.
- Pharynx inf.: → post pharynx & Tonsillar area.
- Skin inf: → pustule.
- DGI ← Joint / CSF / Blood.

* Swab:

① If urethra swab → ٢-٣ سم بتدخل جوة عشان في عايشة بي اكثر
② Swab: ↓ platinum or Ca+ alignate or Rayon
(Not Cotton d.t bactericidal)

فاخد عينتين ← Stain / Culture

③ 2 hrs. after urinat.
Then: . Gentle spread over slide
air dried or Heat fixed

Direct MIC. exam: OIF exam: if ≥ 4 PMNL/HPF → Urethritis

Stain (٣ أنواع)

- Gram stain → Gram -Ve, Kidney shapped Intracellular Diplococci (inside PMNL & EPith. Cells.) (Pink) red
- MB × false result
  - Rapid But:
  - ① don't show staining properties as Gram.
  - ② Need special Conditions (Transport & 4°C)
- Immuno-Fluorescence. ×
  - Sensitive But
  - Not specific

Not Specific (detect live & dead) so Not used in Prognosis.

• Predictive Value: of Gram stain: (Sensitivity):

Good in:
- Symptomatic ♂ inf (urethral)
- Conjunctival Inf.

Low in
- asymptomatic ♂ ("during screening")
- females (Endocervical inf.)
- Extragenital Inf: Rectum, pharynx, skin, DGI. (Except Conjuctiva)

DD of Gram -ve stain organisms in the specimen:

① Denaturated staph, lost their stain & become G-ve.

② Short Coligerm bacteria: in ♀ genitalia. (E.coli)

③ Moraxella & Actino bacter group.

Technique of Gram Stain:

Stain ē 1% Crystal Violet
↓ rinse ē Water (after 20 sec)
Add Gram's Iodine
↓ rinse ē water (after 20 sec).
Remove the stain.
↓ rinse ē water
Counter stain ē (Neutral red)
↓
Examined.

3. **Culture** (Most Accurate For ✓ sensitivity 90% & specificity 95%)

(A) • Indications:

1. Asymptomatic Males
2. Females (Endocx Inf.)
3. Extragenital Inf: (Except conjunctiva):
   - Rectum
   - pharynx
   - Skin
   - DGI
4. doubtful diagnosis.
5. Medico legal Conditions (Rape or Abuse)

Stain

(B) Sensitivity:

Source of the sample	Diagnostic sensitivity	
	Gram stain	Culture
① Symptomatic males	98%	98%
② Females and asymptomatic males	50%	95%
③ Conjunctiva	95%	95%
④ Pharynx, rectum and blood in disseminated infection.	Not recommended	25-75%

Extra-genital

(C) Media (...)

- **Transport Media** (stuart's Media)
  - Can viable for 1-3 d
  - Ex: Agar, NaOH, Glycolic acid.
  - MB
- **Growth Media** (Enriched)
  - Blood agar (inhibitory for ...)
  - Pick up: HB, CO2
  - Non Selective
    - Chocolate agar
    - Lysed Blood
    - (Mcleud's Choclate agar) 80°
    - Blood agar
  - Selective
    - Thyer-Martin Media (TMM)
    - New York Media
    - mcleud's
    - Blood agar Anti microbe
- **Growth Transfo Media** (Biologic Environmental Chamb)
  - Modified Thyer Martin
  - Mod. TMA

N.B: Enriched Selective media ±

① Antibiotic Containing (Thyer Martin):

- Vancomycin → -- G+ve
- Nystatin → -- Yeast
- TMP → -- proteus
- Clistemidate → -- G-ve.

(Trimethoprim)

② Selective New York Media

The following needed for Culture:

- CO_2: 5%
- Moisture: 70%
- Temp: 36 °C

↓ 48 hrs (لا تنتظر نتيجة إيجابية أكثر من 72 ساعة)

Colonies: Glistening, Soft, Rounded (0.5 mm - 2 cm)

↓ 4 Types

① Type I & II ← Small, Pigmented, Pili (Fimbriae) → Pathogenic

② Type III & IV ← large, unPigmented, No pili → Non-pathogenic

Anti biotic sensitivity (In one study (2007) on 60 strains isolated from 62 Pt)

- all strains susceptible to: Cefixime, Ceftriaxone, AZithromycin, Spectinomycin.
- Some strains are resistant to: Cipro., Penicillin, Tetracycline.

4. Biochemical & Nutritional Tests

Oxidase Reaction

- Non Specific (+ve in Pseudomonas, Haemophilus)
- Detect Gonocccal Colonies in Mixed Cultures
  - Add oxidase Reagent (4-methylpara phenylene)
  - Gonococcal Colonies: Turns pink - Purple.

Fermentation Reaction

- 4 of: Glucose, Maltose, Lactose, Sucrose added to the Culture
- \+ phenol red Indicator (if Acid production) (if Fermentation: Red → Yellow)
- Used to: detect N. Gonorrhea in areas Contaminated e^ other strains e.g Rectum & pharynx.

Auxotyping (Auxo = growth)

Classification system For detection of Nutritional requirments of N. Gonorrhea.

It was found That Neisseria G. that depend on AUH in Their Nutrition may be ass. e:

1. urethritis.
2. dissiminated Inf.
3. Penicillin Sensitivity

Gonococci doesn't ferment maltose
meningitidis → ferment maltose

Results:

N. gonorrhoeae	→ Glucose only.
N. meningitidis	→ Glucose + Maltose.
N. lactamica	→ Glucose + Maltose + Lactose.
N. pharyngis sicca	→ Glucose + Maltose + Sucrose
N. catarrhalis	→ No fermentation.

NB: Auxotyping was done by Testing the strains For Their requirments For: (8)

- Arginine
- proline
- Uracil
- Hypoxanthine
- Serine
- Iso Coline
- Cysteine
- Cystine.

So → N. G → Classified into 8 auxo-Types → Peri → non requiring. / NR 4or. / arginine requiring / proline requiring

5 Antigen detection

- used to: detect gonorrheal Ags in (Fluids) Collected From penis or Ce-vix.
- done by: ELISA
- disadv.: less accurate than Culture.

6 Gene detection (Biological detection)

- Indications:
  1. Specimen transported over long period.
  2. Suboptimum Culture Conditions.
  3. Concomitant chlamydial diagnosis
  4. done on Body Fluids; So useful in Conditions in ♀ there is difficult in obtaining Mucosal swab (children)
  5. ∴ Culture in medico-legal Conditions.
- Adv.: sensitive & specific as Culture.
- disadv. 1. don't provide Antibiotic susceptability ∴ Culture.
  2. less accurate in presence of Blood or Menses.
  3. Needs longer times.

- Types:

Nucleic Acid Hybridization Test (DNA probe test)

- Special probe used to detect gonorrheal DNA in the Specimen.
- NB: Not Accurate in Throat Sample.

Nucleic acid Amplification Tests (NAATs) (non culture test)

done by: PCR or LCR

NB. Rapid > Culture
. don't require viable organisms.

7. Other Tests.

(A.) Serological Tests e.g ELIZA, RIA & Coagulat- test.

- Value → (Carrier) detection among high risk groups.
- disadv → high antigenic protein varieties.
- classif → gonococci are classified Acc. to Antigenic variations of the proteins on the outer cell memb. into:
  - 3 Serotypes:
    - ① WI
    - ② WII
    - ③ WIII

  → Then subclassificat- may be done using Monoclonal Antibodies.

- Coagulate test (Rapid Slide test)
  - Staph coated e Antigonococcal Abs + Gonococcal suspension
  - ↓
  - Agglutinate (granular)

(B.) Other Invs. For detection of other STDs e.g HIV, chlamydia ✓ (associate - 50% of Gonorrhea).
↓
Syphilis

7. Other Tests.

A. Serological Tests e.g ELIZA, RIA & Coagulase test.

- Value → Carrier detection among high risk groups.
- disadv → high antigenic protein varieties.
- Classif. → Gonococci are classified Acc. to Antigenic variations of the proteins on the outer cell memb. into:
  - 3 Serotypes:
    - ① WI
    - ② WII
    - ③ WIII

  → Then Subclassification may be done using Monoclonal Antibodies.

- Coagulase test (Rapid Slide test)
  - Staph coated w/ antigonococcal Abs + Gonococcal suspension
  - ↓
  - Agglutination (granular)

B. Other Invs For detection of other STDs e.g HIV, chlamydia ✓

- ↓
- PCR ✓
- (associate - 50% of Gonorrhea).

Treatment of Gonorrhea

① General Measures:

- No intercourse for 2-4 wks.
- Both partners should be Treated at the same time.
- avoid: Alcohol, Exertion → may cause "Traumatic Urethritis"
- avoid: Self etam., local anesthetics → may cause chemical urethritis

② Antibiotic therapy:

- [A] Recent Ht: According to CDC 2010
- [B] Old Ht: Not recommended Nowadays due to resistance

Ideal Antibiotic should be:

- Effective.
- low cost.
- No: Allergy, Toxicity, pregnancy complications
- Effective against: chlamydia & gc → So not masking it

Ht of chlamydia: (ass. gonorrhea in ≃ 50%)

- Azithromycin (1gm) → Single dose
- or Doxycycline (100) → (1 x 2 x 7)
- Erythromycin.

+ Flagyl for trichomonas.

Ceftriaxone (IM) → Antibiotic

A CDC Updated recommended treatment regimens for gonococcal infections and associated conditions - United States, 2010

1. Uncomplicated Gonorrhoeae of Urethra, Cx or Rectum:

Recommended Regimen

- Ceftriaxone 250 mg IM (single) (فقط)
- or Cefixime 400 mg (أو) (Ximacef 400 Caps)

Alternative Regimen

- Spectinomycin → غير متوفر
- or Cefuroxime (1gm single)
- or Azithro. (2gm single). ؟

2. Uncomplicated Pharyngeal Infx → Ceftriaxone 250 mg IM (Single) + Azithro (1gm Single) or Doxy 7d

3. Gonococcal Epididymitis: → 250 mg Ceftriaxone IM (Single) + (Doxy) 100 x 2 x 10.

4. Gonococcal Conjunctivitis (adults): Ceftriaxone (1gm) single inf + Saline irrigat + Antibiotics Eye oint.

---

uncomplicated → DGI: مرحلية [Hospitalization] [mild ← skin rash, arthralgia, arthritis]

1. IV: الوريدية :- IV Ceftriaxone 1gm /24 hrs until clinical improvement & continue for 24-48 hrs after that. (يوقف بعد تحسن الأعراض)

2. oral: الفموية : "oral" Cefixime 400 mg (يبدأ بعد الوريدية) 400 x 2 x 7d

3. Complicated DGI (Endocarditis or Meningitis)

Ceftriaxone 1-2gm IV (Meningitis: بالتأكيد / Endocarditis: ؟) > مريض لديه (1-2gm/d)

8. Ophthalmia Neonatorum:

A: Prophylactic: 0.5% Erythromycin oint; in Both eyes
Single Application.

B: Curative IM: 25-50 mg/kg (Not > 125 mg)
Ceftriaxone Single Inj.

Tetracycline Silver Nitrate

"No need For Topical"

9. For children Inf:

- Wt > 45 → as adult.
- Wt < 45 → adjust the dose of Ceftriaxone [50 mg/kg]

---

(1) Gonorrhoea in Pregnant

(2) Gonorrhoae

1. Chlamydia
2. Trichomonas

How To avoid Masking of GC by IM??

Antibiotic

Indications of hospitalization:

- initial treatment of (DGI), purulent joint infections, meningitis, and endocarditis.
- initial treatment of PID cases in the presence of the following factors:
  - Pregnancy
  - Failure of outpatient treatment
  - Tuboovarian abscess
  - Severe symptoms (eg, severe pain, high fever, persistent nausea and vomiting)
  - Immunodeficiency
  - Abdominal peritonitis or perihepatitis
  - Uncertain diagnoses, with any possibility of ectopic pregnancy or appendicitis masquerading as PID
  - Uncomplicated urethritis, cervicitis, or rectal or pharyngeal infection in adults

Mechanism of Antibiotic Resistance In Gonorrhea

Chromosomally Mediated

- Mech. Chromosomal Mutations in their genes → ↓ permeability of Gonococcal memb To The antibiotics.
- Leads to: (Partial) or (low) resistance To All Antibiotics.
- Overcome it By: ↑ dose of ".

Extra Chromosomally Mediated (Plasmid)

- Mech. plasmids are an Extra chromosomal DNA Particles that can → β-lactamase (penicillinase enz.) ← بتكسر (lactam ring)
- Leads To: (Complete) or (High) (total) resistance To Antibiotics.
- Overcome it By: Not by ↑ the dose but by changing the antibiotic (penicillinase resistant).

- Causes of tt Failure:
  1. Reinfection (من شخص اتعدى منه او سكس)
  2. Antibiotic Resistance
  3. Post-gonococcal Urethritis (PGU) = d.t untreated Chlamydia
  4. Associated Trichomonas (تريش)

- Follow up of Gonorrhea (Follow up of tt = Tests for Cure)

* At:
  - 2-3 days → stop of discharge (Sign of successful tt)
  - 1 w → Test For gonorrhea & chlamydia
  - 2 ws → Examine for Complications (prostatovesiculitis)
  - 3 ms → Test For ⚥ & HIV.

* Gonococcal proctitis: Seen after 1 w For rectal swab & culture (should be -ve).

أسئلة وقوع شفوي

What is Gonococcal Carriers

- affect 5-10% ♂ Males Infected with gonorrhea « Asymptomatic Inf »
- More common in ♀ (50%)
- ♂: يحتاج لسبل جدان سائل لمنوي لـ
  If little Muccopus ← وجود
  Can be "milked" From meatus & shreds are present in urine → the condition more liable to Complications.
- Asympt. Cases usually d.t (AUH) Arginine uracil Hypoxanthine

why Inf. doesn't give life lasting Immunity ??

1. short IP (short Antigenic Time Exposure)
2. Weak Immunity (OPA protein)
3. Heterogenous Antigenicity ♂ organism: ← high variety
   d.t 3 different OM proteins (PII) So 3 different strains are recognized during reproduction ♂ These strains GPII Constantly changed.
4. Early antibiotic Tt → Const. ♂ (local) Immunity
5. Trichomonas Vaginalis: may act as phagocyte To N. Gonorrhoea That Can live inside Trichomonad & undergo division & despite antigonococcal Tt → relapse
   So Trichomas may serve as reservior For gonococci in Cases ♂ Mixed Inf. & Cause relapse.

III Chlamydia Trachomatis

(Human)

↓

There are 15 Serotypes (BY MIF)

affecting 2 Systems

- **Eye** (A, B, Ba & C) → Trachoma
- **Genital System**
  - **Mucosal** (Non Invasive) (Serotypes D-K) → non gonococcal urethritis
    - (1) NGU
    - (2) Reiters Synd.
    - (3) Others
  - **Lymphatics** (Invasive) (L1) (L2) & (L3) → LGV lymphogranuloma venereum

- Taxonomy
  1. Species
  2. Serovars (based on OCM-proteins) (A – L3)
  3. Biovars: LGV als Vs Non LGV als.

Life Cycle:

- requires 36–48 hrs.
- has predilection To Columnar Epith but LGV strains Can infect St. Sq. Epith.

• Life Cycle of Chlamydia

Involves 2 Morphological Forms

(Inclusion = Initial) تشبه الإسم

Elementar Body (EB)

- Extracellular phase
- Rigid cell wall
- doesn't replicate
- Infectious

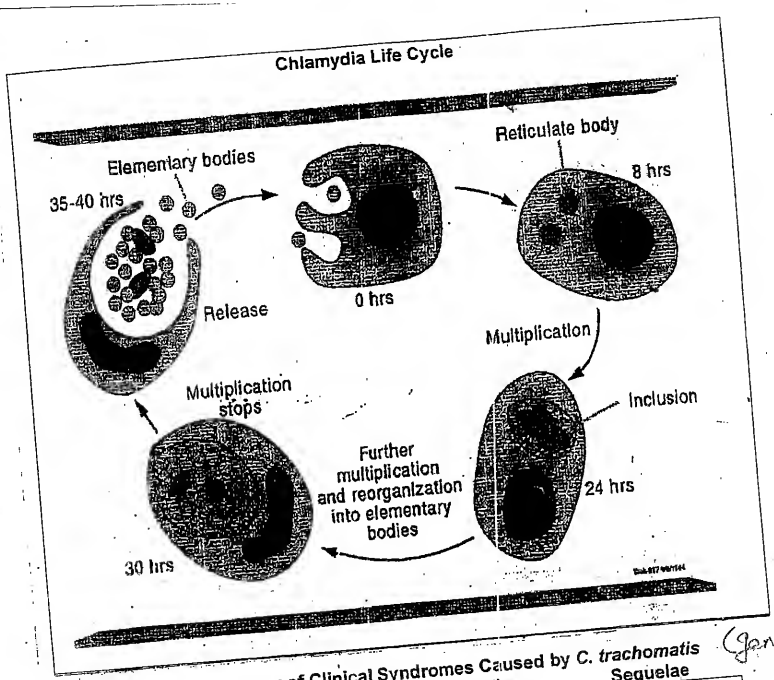
Reticular Body (RB)

- Intra cellular phase
- fragile CW.
- adapted for growth & Multiplication
- Not infectious.

Pathophysiology:

- EB attaches To the Cell Epithelium → phagocytosed Inside phagocytic vacuole → failed phagolysosomal destruction (No Known Act.)
- EB: Inside the phagocytic vacuole يتحول → RB → grow & multiply by binary Fission.
- RB Then → multiply & Fill the cytoplasm (Inclusion Body)
- Then Inclusion Body → organize into (EBs) → Cell lysis & release of Infectious (EBs)

(See diagram)



Summary of Clinical Syndromes Caused by *C. trachomatis* (genital)

	Local Infection	Complication	Sequelae
Men	Conjunctivitis	• Prostatitis • Epididymitis • Reiter's syndrome	Infertility
	Urethritis		
	Proctitis		
Women	Conjunctivitis	• Pelvic Inflammatory Disease • Perihepatitis • CIN • Reiter's syndrome • pregnant → Abort.	Infertility Ectopic pregnancy Chronic pelvic pain
	Urethritis		
	Cervicitis		
	Proctitis		
Infants	Conjunctivitis	Chronic lung disease ?	
	Pneumonia		
	Pharyngitis Rhinitis / OM		

Male Infections

A. Urethritis (NGU)

Male Urethritis (Ingenoral) → Male: GU, NGU

def. Urethral Inflammation can be: Infectious or Post Traumatic

Causes

- Gonococcal Urethritis (GU) (less common)
  - Known Etiology (75%)
- Nongonococcal Urethritis (NGU) (More common sp. — less promiscuous, high socioeconomic, heterosexuals)
  - Unknown Etiology (25%)
    - Non specific urethritis (NSU).

A. Common Causes:

- C. Trachomatis (D-K) (30-50%)
- Ureaplasma Urealyticum (20-40%)
- Mycoplasma Hominis (5-10%)
- Trichomonas Vaginalis (<5%)

B. Less Common Caused:

- HSV
- LGV, Lymphogranuloma venereum.
- ♂
  - Staph. Saprophyticus
  - Staph. Viridans
- CMV
- Adenoviruses.

- UTI
- Urogenital TB
- SJS
- Acute Hgic Cystitis.
- Traumatic:
  - FB
  - Instrumentation
  - Stricture
  - Stones
  - Oxaluria & Phosphaturia

Non venereal causes of urethritis.

CIP of non-gonococcal urethritis

- Asymptomatic → 50%
- Symptomatic cases may be presented with:

Sexual / Instrumentation (Hx of)

- IP: 2 days - 4 wks (usually 2-3 wks)
- Discharge: ch BY:
  - Thick
  - Scanty
  - Mucoid, Purulent or Mucopurulent
  - oral: green, yellow, Brown or Blood Tinged
- Dysuria: ch BY:
  - localized to meatus or distal penis
  - Worst during First morning Void (AM)
  - ↑ ē Alcohol
- urgency & Frequency: Typically absent & if present will suggest Cystitis / Prostatitis
- Itching: sense of Itching or pruritus that persist bet. voids. affect the urethra / Urethral / Bet. voids.
- Orchalgia: Heaviness in the Genitalia & ass. pain in Testicles → suggest Epididymitis or orchitis.

- Complications: → Epididymorchitis, prostatitis Reiters.
- Sequelae: → Infertility.
- NB: there is Tendency For recurrence & chronicity.

Difference bet GU & N GU: NG (ch BY)

- IP > GU
- Disch. Scanty / Thick / Purul. or Muco Purul. / oral
- Cause: →

NB Types of urethritis

1. GU
2. NGU (subtype of NSU)
3. Postgonococcal urethritis:

Type of urethritis Ch'By

Start as GU + NGU (Chlamydia / Inf. usually ass. Gonorrhoea)

↓

Patient receive effective Rx For Gonorrhea & Not For Chlamydia

↓

So after long period (IP in chlamydia is longer) after treating GU → PGU.

So

Any Case of GU → Treat Gonorrhea & Follow this Rx by Antichlamydial Course.

Incid of Chlamydia in:
- PGU (80%)
- NGU (50%)
- GU (30%)

4. Recurrent or Persistent NGU:

def NGU that < has ≥ 4 attack / Year after full Rx
or doesn't respond completely to Rx

Incid: 10% NGU.

Aetiology:
1. Insufficient antibiotic Rx.
2. Resistant Antibiotic: Tetracycline - resistant U. urealyticum or T. Vaginalis.
3. Reinfection (partner)
4. Latent chlamydial Inf.
5. organism protected in sites as prostate
6. Excess alcohol / Psychological: anxiety & frequent recurrent NGU.
7. UTI
8. Urethrophobia

NGU

Women Inf. by Chlamydia

♀ Genital Inf. Includes:

Cervicitis

- usually Asymptomatic (70-80%).
- when symptomatic → Non specific Symptoms as low back pain.

Specific signs (5-10%) may include:

- Mucopurulent endocervical discharge.
- Easy cervical Bleeding

Urethritis

- usually asympt.
- Similar to ♂ urethritis
- Manifs. Worsened during Menses.
- May Cause dysuria - Pyuria Synd. mimicking "Cystitis".

- Complications:

① PID → Chr. pain ✓ "ectopic!" / Infertility ✓ / Ectopic pregnancy.

- may be Asympt.
- Milder Than That of Gonococcal inf.

② Perihepatitis: (Fitz Hugh Curtis Synd).

③ Pregnant → Abort

④ CIN

⑤ Reiter's.

- diseases seen Both in ♂ & ♀

① Conjunctivitis (Inclusion conjunctivitis)
- subinfolliculation.
- Follicular & Non purulent (Seropurulent) } ≠ Gono Gccal → purulent

② Proctitis:
- d.t (Non) L GV Serovars.
- AET ♂ : Homosexuality / ♀ : Anal sex or Complicating endocervitis.
- CIP

Gonorrhea ≠ CI

③ Reiter's dis. = Reactive Arthritis (RA)

(Venereal Arthritis = Sexually Acquired RA)

① urethritis (or Cervicitis / Colitis) — in children (♂ > ♀)
② Arthritis — d.t C. Trachomatis (D-K)
③ Conjunctivitis
④ Keratoderma Blenorrhagicum & Circinale Balanitis / Vulvitis

def: Episode of Arthropathy occuring within 1 month of an episode of urethritis, Cervicitis or Colitis

.. AET (Unknown)

① Genetic → HLA B27

② Infective:

- Post Venereal (3) → NGU (1-4%) > GU (Commonest → C. Trachomatis); Mycoplasma
- Post dysenteric → Shigella & Salmonella
- Others → Strept viridans, Mycoplasma pneumoniae

CIP

Usually Following Inf. of 3

① urethritis
② Cervicitis } C. Trachomatis > Gon.
③ Colitis — e.g Shigella & Salmonella

3 Main Manifs.

① Articular
② Ocular
③ Mucocut.

3 Rare Manifs

① CNS
- Meningitis
- Encephalitis
- death ?? ← Aortitis / Amyloidosis

② CVS
- Carditis
- Aortitis

③ Systemic
- Generalized L.N
- Thrombophlebitis
- Amyloidosis

Arthritis:
↓ C. Trachomatis
Reactive (Immunologic)
But
d.t Gonorrhea is d.t dissiminate from urethra to Joint

① Articular → Poly-arthritis (h-Cy)
- Non suppurative.
- ē in 1 m ♂ Urethritis or Cervicitis or colitis.
- Commonest joint → Sacroiliitis (Pain at back & buttock; ↑ by rest.
- Other Joints:
  - Knee → Pain, Tenderness & Effusion.
  - Small finger joints → . Fusiform dactylitis . Tenosynovitis . Sausage digits.

② Ocular → usually Conjunctivitis.

③ Mucocut.: ٣ حاجات تتعطوا كويس
- Oral ulcers
- Keratoderma blenorrhagica (Waxy) ↓ scaly
  - Psoriasiform erythematous lesions that begin as Vesicles on Erythematous base
  - Progress To → Macules, Papules & Nodules
- Circinate Balanitis & Vulvitis
  - "Painless" Erosive dermatitis ē small ulcers on glans & Vulva.

Invs
① ⊠ ♂ specific bact. inf. < Chlamydia, Shigella, ...
② Arthrocentesis: to Exclude bact. Arthritis.
③ Acute Cases
- Neutrophilia
- ↑ CRP
- ↑ C3 & C4
- ↑ ESR

④ Chr. Cases:
Normochromic ✓
Normocytic Anemia

Site: PP. / Scrotum & Nail / Scalp / Trunk

Treatment
Oral Cs → No Effect
& Corticosteroids
① Urethritis & Colitis → Antibiotics
② Arthritis: NSAIDs (Indomethacin)
③ MTX & Azathioprine

Infants & Children Inf.

Inclusion Conjunctivitis

- IP: 5-14 ds
- Mucoid → Copious purulent discharge.

Pneumonia (Afebrile Pneumonia Synd)

- 1-3 ms after delivery

- Most genital & rectal Inf. ± Asympt.

Mode of Transmission:

1. Sexual Assault
2. Vertical Transmission: From vagina during delivery may remain Latent for 2-3 yrs.

Neonatal Conjunctivitis (Ophthalmia Neonatorum)

- WHO def. Any conjunctivitis ± discharge occuring during the First 28 days of life.

Gonococcal

- less common but more serious.
- IP: 3-5 ds
- Bilat. Hyperacute with purulent discharge.
- May → Corneal ulcer → perforation & blindness.

NB. other causes: Chemical (Silver Nitrate) / Viral (HSV).

Chlamydial trachomatis

- Most Common & less serious.
- 5-14 ds
- unilat. or Bilat Watery discharge That become Copious & purulent later
- usually mild & self limited.

Diagnosis of Urethritis

2 steps: ① Dx of urethritis ② Dx of AET

الخطوة الأولى → • Urethritis can be diagnosed based on one or more of the following:

1. Purulent or Mucopurulent urethral discharge. (Chlamydia)
2. Urethral Swab or Exudate → ≥ 5 WBCs / OIF (oil immersion Field)
3. First voided urine that show:
   - WBCs esterase on dipstick test
   - or ≥ 10 WBCs / HPF.

الخطوة الثانية → • Then: All patients with urethritis should be Investigated For NG & C. Trachomatis

- Invs for Gonorrhea → ...
- Invs for C. Trachomatis:

1. Culture Techniques
2. Antibody detection < IgG / IgM
3. Antigen detection < ELISA / DFAT
4. Gene detection < DNA probe test / NAATs

Specimen

أفضل العينات هي: Swab, urine, Discharge

بالترتيب ↑ Can be obtained for:
- Gram stain
- Culture
- IF
- Enzyme assay
- NAATs

NB. Urine specimen: Not used for Diagnosis of urethritis Except:

Dysuria + No Discharge → (1) To Exclude Cystitis or Pyelonephritis
↓
?? Cystitis / PN
↓
(Urine analysis)

ω is necessary if there is Dysuria without discharge.

(2) if used for NAATs. → "nucleic acid amplification test"

(3) if " " ⊘ & T. Vaginalis.

Also patients ♂ ← GU: may have WBCs in Voide ♂ few or no mid's
NGU
≥ 30% No WBCs Urine.

Swab شروط
(1) Ca alginate on non wooden stick
(2) 2 hrs after urination
(3) 2 cm introduced in urethra.

A. Culture Technique

Swabed Epithelial cells → Transport Media → Inoculate into Culture cell Monolaye

From Urethra / CK(♀)

Not Secretions Because C. is obligate intra cellular So present in scrapped material rather than discharge or urine.

MC Cop Cells (Treated by Cycloheximide & Contain sucrose).
كلوروهكسيميد
يحتوي على سكروز

Treated or anti (To -- on the cul

Cells ناقل Chlamidya → Inter cellular

48 hrs → Staining: .Geimsa .Iodine .IF., Direct Immuno fluorescence → Intra Cellular Chlamy Inclusion Bodies.

. Adv. of Culture: Sure diagnosis
may be used < pre tt → detect sensitivity
post tt → " Cure.

- disadv. of Culture:
  1. High cost
  2. Not available in all labs.
  - not yet standardized
  - time consuming

2. **Antibody detection (Serology):** ⇒ complement fixation test
   - done By: CFT or MicroIF. to detect Antichlamydial Antibodies.
   - Adv & disadv.: of little significance d.t high prevalence of IgG against chlamydia among the populations.
     - But if There is: IgM Abs / 4 times ↑↑ in IgG → diagnose:
       - (A) Complicated Cases. as Chlan Epididymitis, salpingitis & perihepatitis.
       - (B) & C. pneumoniae

3. **Antigen detection (Protein detect):**
   - done By: ELISA (Chlamydia Zyme Test) / DFAT (MicroTrack test) ↳ Direct fluorscent Ag test
     - Sensitive, Specific → good correlate of Culture.
     - Cheap, Easy → can be done on dead organisms.

4. **Gene detection:** By either
   - (A) DNA probe test (Nucleic acid Hybridi. test) → detect chlamydia specific Nucleic Acids.
     - Non Amplified tests.
   - (B) NAATs (Amplified Tests).
     - DNA of chyl.
     - nucleic acid amplification test

B NAATs (Amplified tests) (يعني بيبحث بسالبتين)

By: PCR, LCR

Specimen: Swab or Urine → Non Invasive

Most sensitive & specific.

Can diagnose Both: Gonorrhoea & C. Trachomatis at same Sample.

d ligase chain reaction

NB

. Why ## is difficult Compared to Gonorrhea: ??

① Compliance: Antibiotic in: GU → Single dose; NGU → Multiple doses.

② Cure Rate: In: Gonorrhea: 95%; Chlamydia: 80%

③ Culture: In Contrast to gonococcal culture, chlamydial cultures are: ① Expensive ② Time consuming ③ Not Always available

Lymphogranuloma Venereum (LGV)

(Esthomene, LG Inguinale, Nicolas Favre dis)

- def STD: affect mainly the lymphatic system & caused by C. Trachomatis Serovars (L_1, L_2 & L_3).

- Mode of Transmission:
  1. Sexual: Vaginal sex / Anal sex / Oral sex
  2. Non Sexual: (less common):
     - Fomites
     - Nonsexual Contact
     - Lab. accidents (inoculation)
     - Inhalation (Creation of aerosols of the organism).

- Sex: in ♂ 6 times > ♀. (but complications in ♀ > ♂ (3rd stage) d.t painless hidden Nature of dis.)
- Endemicity: Endemic in: Africa, India, South America

- Pathogenesis:
  - The organism enter the body via microscopic defects in genital Mucosa & Skin → enter Lymphatics → Lymphangitis → Lymphadenitis → Perilymphadenitis & affection of Multiple Neighboring L.Ns → abscess Formation → rupture → Fistulae & Strictures.
  - In Rectum → destruction & ulcerate.
  - Systemic affection: may occurs.

CIP جلد ٢

- Primary Stage → Iry. or Intial manifs (Cutaneous Invasion) بجيث :
  (only in 25% of patients).
  - Ip: 3-12 days.
  - There may be:
    1. Primary lesion "Painless" / papule, Herpetiform vesicle, بثرة pustule, or ulcer
       - Ch / small Transient Lymphangitis & / Genital swellings
       - Site / ♂: Coronal Sulcus, Glans, Intrameatal → discharge. / ♀: Vagina or Cx, Vulva (last war) / ♀ & Homosex: Rectum.
    2. Non Specific / Urethritis / Cervicitis / Proctitis.

- Secondary Stage → Inguinal Synd (بوبك) (Lymphatic Invasion) بجيث :
  - occurs after: 1a-3o ds - 6 ms. (2ws after disappearance of 1ry stage).
  - Include 3: أو
    1. Buboes: (unilat) (70%), Enlarged Painful, Matted Inguinal L.N (Fused Multiple Abscess) Tender
    2. Groove sign: (chic): The Inguinal L.Ns Form 2 groups above & below ing. ligam (ي) Forms groove bet. Them. (30% 2 Pts)

NB

1. Inguinal Synd. is unusual in Females as the draining L.Ns of Vaginal & Cervix are deeply seated in pelvis.
2. Constitutional Manifs: Common e.g FAHN, EM, EN
3. Systemic Spread of C.T → Pneumonia & Hepatitis.

③ Watering Pot or Poradenitis: L-Ns become matted → Fluctuate → break through the Inflammed SKin → Chr. discharging Sinuses.

Tertiary Stage

Genito-Ano-rectal Syd (♀>♂) (Lymphatic obst)

- occurs after: ms - ys.
- Sex: ♀>♂ d.t spread From vagina to rectum (or) d.t Anal sex. ♂ → Homosexuality

Include:

① Elephantiasis ♂ < Genitalia < penis, vulvae. ♀ < L.Ls

② Proctocolitis (granulomatous) < Scarring Stricture fistula of Thigh, buttocks, urethra.

③ end stage < Ethiomene (vulval elephantiasis + Fistulae); Sexophene (penile Elephantiasis + Fistulae)

④ ... → Cancer SCC

Note:
- Inguinal Syndr ♂>♀
- Genito ano-rectal Syndr ♀>♂

Cause of Death:
- proctitis → perforation → Peritonitis
- Cancer

Other manifs:
- FAHM
- Arthralgia
- Meningitis & Encephalitis, pneumonia
- SKin Rash.

Inv:
① Frei test: Intradermal test (discontinued in 1974) Ag (Lygranum): containing Killed Agent → papule > 0.5cm
② CFT: sensitive (titer ≥ 1:16)
③ MIF: More sensitive & specific (titer ≥ 1:512)
④ NAATs: PCR, LCR & (recently) Multiplexed Real Time PCR.
⑤ Histopathology
⑥ Bubo Aspirate & culture (cell culture): 30% of Cases

Most Specific & Sensitive

Micro immuno fl

inverted Frei test ??

Treatment (2006 CDC STD Treatment Guidelines)

A. Treatment of uncomplicated genital chlamydial infections:

1. Recommended regimens:

Azithromycin, 1.0 gram orally in a single dose, or
Doxycycline 100 mg orally twice daily for 7 days (*Some strains resistant*).

2. Alternative regimens:

Erythromycin base 500 mg orally four times a days for 7 days, or
Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days,
or
Ofloxacin 400 mg orally twice a day for 7 days, or
Levofloxacin 500 mg orally once a day for 7 days.

B. Treatment of chlamydial infection in pregnant women:

1. Recommended regimens:

Azithromycin 1.0 gram orally in a single dose, or
Amoxicillin 500 mg orally three times a day for 7 days.

2. Alternative regimens:

Erythromycin base 500 mg orally four times a day for 7 days, or
Erythromycin base 250 mg orally four times a day for 14 days, or
Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days, or
Erythromycin ethylsuccinate 400 mg orally four times a days for 14 days, or

NB. Erythromycin estolate is contraindicated during pregnancy because of drugrelated hepatotoxicity.

C. Treatment of neonatal conjunctivitis and/or pneumonia:

1. *Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into four doses daily for 14 days.**
2. Prophylactic antibiotic treatment for infants born to mothers who have an untreated chlamydial infection is not indicated. Infants should be monitored to ensure appropriate treatment if infection develops.

D. Treatment of chlamydial infection in children:

1. Children who weigh <45 kg:
Erythromycin base or ethylsuccinate 50 mg/day orally divided into four doses daily for 14 days.

2. Children who weigh > 45 kg, but are < 8 years of age:
Azithromycin 1.0 gram orally in a single dose.

3. Children ≥ 8 years of age:
Azithromycin 1.0 gram orally in a single dose, or
Doxycycline 100 mg orally twice a day for 7 days.

E. Treatment of lymphogranuloma venereum:(ثلاث اسابيع)

1. Recommended regimen:

Doxycycline 100 mg orally twice a day for 21 days.

2. Alternative regimen:

Erythromycin base 500 mg orally 4 times a day for 21 days.

NB. Some experts believe azithromycin 1.0 gram orally once weekly for three weeks is likely to be effective, although clinical data are lacking.

NB

No clinically significant emergence of drug resistance among CT strains. G. Patients should be instructed to abstain from sexual intercourse until partners are cured and for seven days after a single dose of azithromycin or until completion of a seven-day treatment regimen.

**Repeat testing after treatment for a chlamydial infection.*

1. Pregnant women: repeat testing, preferably by culture, 3 weeks after completion of therapy.
2. Consider test of cure 3 weeks after completion of therapy any time erythromycin is used.
3. All women with chlamydial infection should be encouraged to return for repeat screening approximately 3 months after treatment. Some experts also recommend men with chlamydial infection undergo repeat screening at approximately 3 months post-therapy.

The following antibiotics not used

1. Penicillin:very large dose needed/day (30 million/d).
2. Rifampicin: effective in vitro but resistant strains develop.
3. Aminoglycosides and cephalosporins (not effective).

Bacterial Vaginosis

(Non Specific Vaginitis)

Def: Polymorphic Synergistic Inf. that may affect:

1. Women → Colonization &/or Inf. of Vagina
2. Men → Colonization of urethra (in men whose their Sexual partners have BV)

AET: This Polymorphic Synergistic Inf. is d.t 2 factors:

1. ↓ Lactobacilli (NL Vaginal Flora) (± d.t) — Antibiotics, change pH
2. ↑ Anaerobes:
   - A. Gardenerella Vaginalis [ ]
   - B. Anaerobes (other) — Mycoplasma Hominis, Pepto Coccus, Sbepto Cocci Viridans, Backeroides species

[Non motile, Non Flagellated, G-ve Rods.]

Pathophysiology:

NLLY: Lactobacilli are present in Large No in the Vagina → libration of H_2O_2 → Acidic pH (4-5) in vagina → -- growth of Anaerobes.

In BV: There is ↓ in No of Lacto bacilli → ↑ PH → ↑ Gardenerella & other anaerobes.

Epidemiology:

- Age & Sex: all ages & Sexes
- Boys & girls → Colonization
- Women (Adult) → Colonization &/or Inf. of Vagina
- Men → Colonization Not Infection Affect urethra of 80% of MEn whose wife (Sexual partner) having BV.

Sexually transmitted ICD

D Mode of Transmission:

→ Sexually Transmitted (STD / يعني لازم يكون جنسي)

Clp = Amsel's Criteria For D. (3 Needed For D)

① Discharge of D by:
- Smooth, Homogenous & grayish-white.
- Fishy smelling (ammonical).
- Specially Noticed after sexual intercourse.
- Lack of Vaginal inflamm. (So better say Vaginosis not Vaginitis).
  - there may be < initial = itching (mis D as candidiasis)

② pH ≥ 4.5 (NL Y < 4.2)

③ +ve amine test: drop of vaginal disch. + drop of KOH (10%)
→ Fishy ammonical odour (d.t release of volatile amines.)

"Whiff test"

④ Clue cell demonstration (Pathognomonic)

drop of vaginal discharge
+
saline drop.
↓
Clue cells (bacteria attached to vaginal Epithelial cells)

* Culture of G. Vaginalis: → (on) Blood agar medium → ① beta hemolysis on human Not horse blood
② Catalase & Oxidase –ve.

Asymptomatic

Complications:

① Sexual dysfunction (d.t bad smell)
② post partum ← Endometritis, Bacteremia, Neonatal inf.
③ pROM & preterm labor (So tt in pregnant women is essential)

Treatment:

① Metronidazole ← 400 mg twice / day x 5d. / 2gm single dose
② if pregnant → Ampicillin 500 x 4 x 7.
③ Clindamycin Cream 2% Intravaginally

routine tt of Sexual partner Not recommended because Recurrence in ♀ Not affected by tt of the ... → معنى دلي لعلاج زوج في نفس الوقت

Trichomoniasis

Def Sexually Transmitted Infection Caused by Trichomonas Vaginalis: usually affect ♀ (in ♂ usually Asymp)

Morph →
- Anaerobic protozoan
- Oval (10 x 7 μm) — after attach to Vaginal epith. → Amoeboid Shape.
- Motile

has (5) structures:
- 4 Flagellae → For movement.
- 1 undulating memb.
- Axostyle → Microtubular structure Needed For ① Tissue attachment ② " damage.
- Trailing (Post) Flagellum.
- Nucleus & Cytoplasm.

Behavior (5)
- Chic Jerky movement
- Gonorrhea cells → infect Sq. Epithelium e.g. Vagina
- Staph → Can phagocytose other organisms (Bacteria, Candida) as Gonorrhea inside Cytoplasmic Vacuoles
- Needs Carbohydrate For their Energy & the Later is present in Vagina.
- Can live For upto 24 hrs in moist environment.

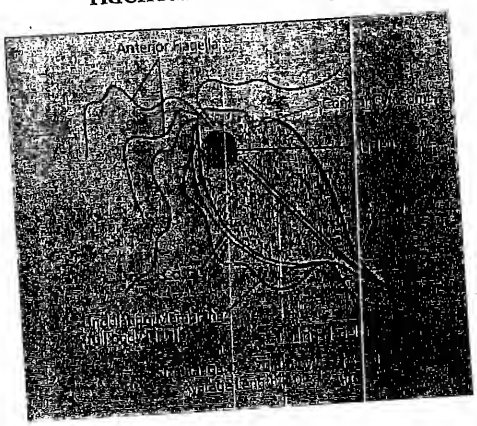
CHo
Movem.
Inf
Phago-cytosis.
Live for 24 hrs in —

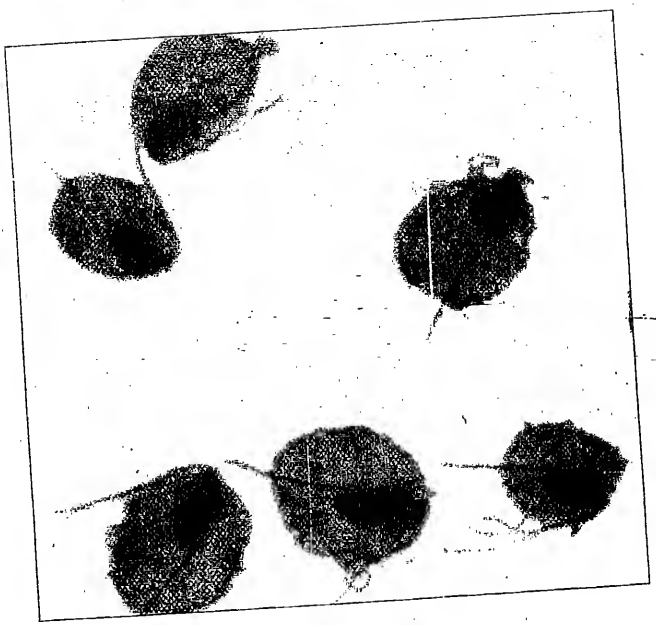
Mode of Transmission:

① Sexual Transmission: from ♀ to ♂

- ♀ Carrier is important reservior For inf. (Vagina is Suitable)
- ♂ " ; is less " " " " because Semen has anti trichomonal properties (Zinc Salts). (Semen unSuitable)

TRICHOMONAS VAGINALIS





② Non sexual Transmission (تقدر تقيس لنا ... بالساعة)

- Fomites
- Lavatory Seats
- Body Fluids < Urine / Semen / Vaginal Exudate.

Intra partum ⇒ uncommon → Neonatal Trichomonal Vaginitis.
Through birth Canal.

Incid: T. Vaginalis Commonly ass. with.
Other Sexually Transmitted diseases:

- Gonorrhoea → 30%
- U. urealyticum → 95%
- M. Hominis → 90%
- Gardnerella V. → 90%

C/P

- IP: 3 days – 3 Ws.

In ♀ → Asympt Vaginitis, Urethritis, Cervicitis, Pregnant, PH

① Asymptomatic

② Vaginitis:
- Discharge: profuse, yellow, irritant, Frothy, offensive. (Menses & pregnancy)
- Inflammed

③ Urethritis (50%) → Dysuria, --

④ Cervicitis: inflammed (strawberry Cx)

⑤ ↑ PH: 5–8.

⑥ In pregnant < Preterm / PROM

In ♂

① usually Asymptomatic

② NGU (5%)

③ ulcerative balanoposthitis

- discharge: Scanty, thick Mucoid or Mucopurulent
- ticking in Urethra chiefly after Coitus.
- Dyspareunia

Diagnosis

1. Direct Mic Exam « Wet-Mounted preparation » (Wet smear)

Most reliable Method

Specimen: Secretions From → Vaginal fornix / Urethra (better scraping)

discharge + Saline → Jerky Movement

+ Saline drop

Dark Field illumination or Transmitted light > نقطة بسيطة ودقيق

Clue: Motile Flagellate + Jerky Movement

2. Stained smear "Papanicolaou" → less reliable.
3. Culture → Fineberg - Whittington for 4 hrs.
4. Exclude Other STDs.

Treat → whole wife has Trichomas to ↓ relief & Further Spread.

Exclude Any STD

Treatment

1. Metronidazole: 2 gm single dose with food.
2. For pregnant → after 1st trimester → Systemic: Flagyl
   before → Topical. Clotrimazole Vaginal Tab.
3. For Infants > 4m.: Flagyl 5 mg/kg x 3/day for 3 days.
4. Failed Metronidazole → Metronidazole Vaginal Pessaries / Betadine Vaginal tab.

Genital Candidiasis

(dimorphic Fungus)

Candida: (yeast like) organism present in 2 forms:

- non pathogenic (yeast) Form: present in
  - GIT
  - Vagina (20%)
  - Rectum
  - Muco Cut. areas
  - Moist intertrigenous areas
  - Urine

- pathogenic (Mycelial) Form: → Causing Candidiasis.

Types:
- Albicans (Commonest 80%)
- Tropicalis
- Pseudotropicalis
- Glabrata
- Krusei

(20%)

- Predisposing Factors:
  - The conversion From nonpathogenic (yeast) to pathogenic (Mycelial Form) may occur under certain predisposing Factors as:
    - DM
    - pregnancy
    - Cs
    - AIDS
    - Antibiotics
    - OCPs
    - Immunosuppressives.
    - Tamoxifen

CIP (may be asymptomatic)

- Female Candidiasis
  - Vulvovaginitis
  - Dysuria & Dyspareunia
- Male Candidiasis
  - Balanoposthitis
  - Allergic form

Female Candidiasis

Vulvo Vaginal (VVC)

- Incid: at attack:
  - (i). 75% of ♀s had an attack during their life.
  - (ii). 30% → ♂ pregnant.
  - (iii). 15% → non "
- C/P
  - Vulva → Tender, painful, Edematous, Erythematous Eroded.
  - Vagina: → discharge:
    - Scanty
    - Thick
    - Whitish (Crude-cheese like)
    - → Cheesy plaques on its walls → if removed → red Haemhegic area.
- 2P
  - pH: → NL (≤ 4.5). (لو زاد التشبع بـ SAS)
  - Premenestrual irritation may occur.

Recurrent VVC ē
No. Known Ppt. Factor;
→ early Sign of HIV

- Patients ē VVC can be divided into 2 main groups:
  1. Single or Few episodes → predisposing Factors can be detected
  2. Frequent Episodes: (≥ 4 Symptomatic & Mycological proven attacks / Year)

Dysuria & Dyspareunia

Vulval & Vaginal irritation →
- dysuria
- dyspareunia
- Severe pruritus.

- Mechanism of Recurrent VVC:

C is useful Clinical Marker.

→ 1. AIDs

2. Candida (Blastospheres) may penetrate deeply into the vaginal wall → protected from Topical ATB & when menses occurs → shedding of Epithelium → reemerge as ... viable organism.

3. Candidal reservior in rectum -

- NB:

. Sexual Transmission of Candida in Women is of Minor Importance.

. Candida is not STD but ♂ Contact should be seen if:

- Symptomatic ♂ inf.
- Recurrent ♀ inf.

Investigations:

1. Direct KoH For < Vaginal discharge / Skin scraping → Gram stain → Gram +ve → Blastospores (Y) / Pseudo or True Hyphae (M)

2. Culture on:

① Sabouraud's agar 1-3 days 37°C → Creamy, Moist Colonies → Mic Exam → clusters of budding cells.

② Maisse Meat agar 1-4 days 37°C → C. albicans show < Rounded refractile Chlamydo Spores.

(this media differentiate bet. Albicans (both)

③ Serum tube test 2-3 hrs → Filaments.

- Chromogenic agars:
  - Albicans ID agar
    - Candida Colonies → blue
    - Other yeast → white or Creamy
  - Chrome agar
    - Albicans → green
    - Tropicalis → Blue
    - Krusei → pink

3. Commercial yeast identification system:
   as
   - API 20 C
   - Auxa color

4. Serology:
   - Agglutinating ± precipitating Abs.
   - depend on Cell wall Ag Mannan (Of little value).

Treatment of VVC

- # of predisposing factors
- Vaginal pessaries (Corner Stone of # despite New Systemic antifungal)
- # of Recurrent of Chr. VC (See below)

① Avoid vaginal trauma:
(as K-Y gel)

② Better Vaginal Hygiene:
- تجنب الحمامات الساخنة جدا.
- استخدام صابون خفيف وطبيعي.
- تجنب المنظفات - الجينز - الملابس الضيقة.

③ ↓ Candidal reservoirs in rectum:
Nystatin oral drops.

④ Control DM, Stop { OCPs, Antib., Tamoxif.

. as

1. Imidazole group. { Clotrimazole, Econazole, Miconazole

   A. Clotrimazole
   - 100 mg I Night X 7 ds
   - or. 600 mg Single Night dose

   B. Econazole
   150 I Night X 5 ds

   C. Miconazole: (1200) mg single dose.

2 Nystatin
100000 U Intra-Vaginal at bedtime for 3 d

Recurrent & Chr. VVC:

Ⓐ - Remove predisposing factors e.g OCPs, Antib-

Ⓑ. Systemic antifungal drugs:

- Ketoconazole : 400 × 1 × 5 ds (ورقيات)
- Fluconazole : 150 mg single dose
- Itraconazole: 600 mg single dose.

Ⓒ. longer course & Vaginal pessaries

(Vaginal) Ⓓ. Boric acid 600 mg/d × 14 ds

Ⓔ Ht of ♂ partner.

NB ① Treatment ♂ partner by either Systemic or Topical Creams is essential

② Pregnant → Treatment by Vaginal pessaries (Systemic is C.I).

③ Resistant cases usually d.t C. glabrata & Not d.t C. Albicans ای is resistant to Systemic Azoles (but) responsive to Boric acid.

Male Genital Candidiasis

2 Forms

Candidal Balanoposthitis

- affect uncircumcised
- intense irritation of glans & prepuce ± Erosion & ± white purulent discharge.

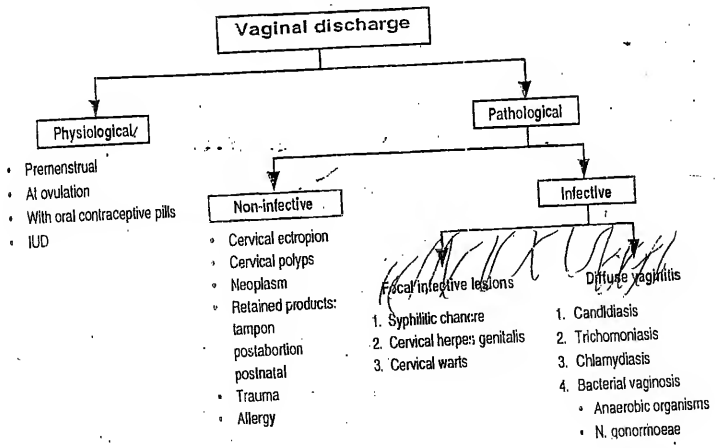
Allergic Form

- Allergic reaction of ♂ partner from infected woman
- ch^r by:
  - itching
  - Burning
  - Small vesicles & Erosion.
- ag → occurs shortly after intercourse

↓

dramatic response to Hydrocortisone is chic.

Vaginal infections



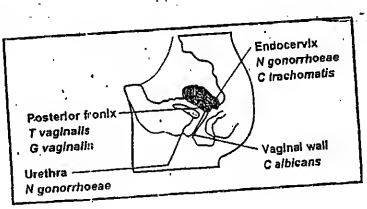
I. History

Certain points in the history suggest that STD is a possibility:

- A recent change of sexual partner.
- Recent multiple sexual contacts.
- Recurrent or persistent symptoms.
- Symptoms in her sexual partner, e.g.
  - Urethral discharge.
  - Irritation and redness of her partner's penis after sexual contact → C albicans.
- General symptoms, e.g. abdominal pain, menstrual problems, rash, dyspareunia, arthralgia.

II. Physical and laboratory investigations

- The **physical signs** and **macroscopic appearance** of a vaginal discharge **do not** help in making an accurate diagnosis.
- Infection can be diagnosed accurately only after **microbiological tests** have been carried out on samples from the **appropriate anatomical sites:**
  - Vaginal wall → C. albicans
  - Endocervix → N. gonorrhoeae, C. trachomatis
  - Urethra → N. gonorrhoeae
  - Post. fornix → T. vaginalis, G. vaginalis



GENITAL ULCERS

1. Genital ulcers.
2. Sexually or non sexually Transmitted genital ulcers.
3. Single or Multiple genital ulcers
4. Painful or painless genital ulcer

1. classification

- Sexually or non sexually Transmitted
- Single or Multiple, Painful or Painless

2. Lab Ø

1. 1st Classification — Genital ulcers

Sexually Transmitted (7)

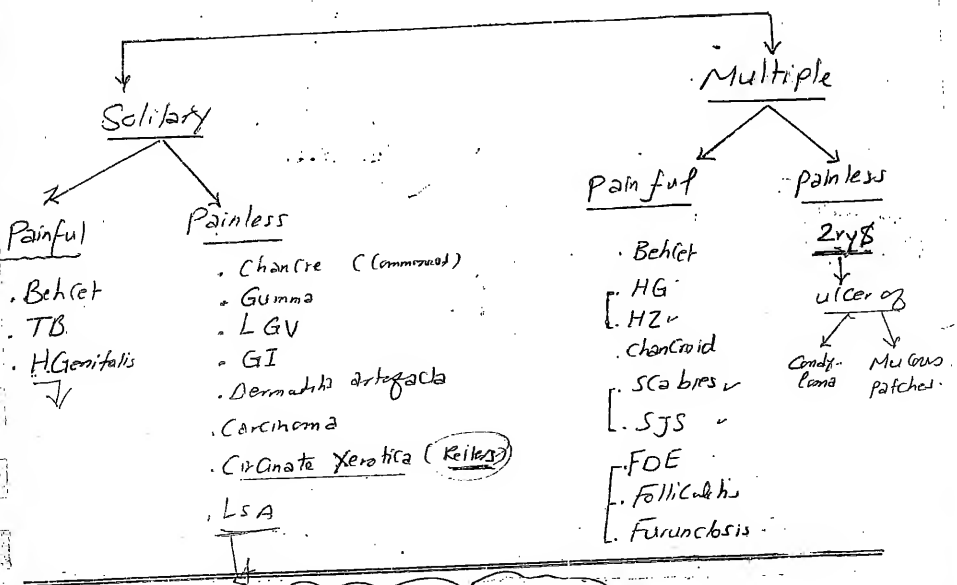
1. Ø → 3 Types of ulcers: Chancre / Snail track / Gumma
2. chancroid
3. Granuloma Inguinale
4. LGV
5. Scabies
6. HSV
7. HIV
8. Others: Gonorrhoea, Trichomonas, Candida.

Non sexually Transmitted 7

1. Traumatic
2. Tuberculous
3. Ø
4. Behcet
5. HZ
6. My
7. FDE. (See Balanitis)

2. 2nd Classification

Genital ulcers



Reactive Genital ulcers

(Ulcers Vulvae Acutum = Lipschutz ulcer)

. Def: Non sexual, non infective reactive genital ± oral ulcerat° that follow an acute systemic illness.

Etiopathogenesis ?? . Exuberant Immune response to the original systemic Inf. DNX EBV

typical

. if recurrent it May be Complex Aphthosis or Behcet dis.

. Cip Acute illness ← Tonsillitis / URTI / diarrhoea of Adolescent girls →

Painful vulvar ± oral ulcers → resolut° → rarely recur.

Inv.: For EBV + EXclude other Causes of Genital ulcers.

Discussion

Dx
- AET
- CIP
- inv.
- HT.

① ♂ → (chancre) (القرحة الصلبة)

② Chancroid → (القرحة الشنكرية)

③ Granuloma Inguinale: (ulcer related to Inguinal area)

④ LGV → ulcer is small Transient & usually not seen & the pt usually presented by Inguinal manifs (syndrome)

⑤ Scabies: ulcers asse < Nocturnal Itching, other Typical lesions of Scabis. [القمل الحكة Scabiasis]

⑥ HSV (Commonest Cause of genital ulcer)
Vesicle → ulcer < Multiple, small, superficial, on Erythematous base. & very painful
[القمل الحكة H. Genitalis.]

⑦ HIV:
- occur in HIV patient
- -ve inv. for other causes < ♂ chancroid / HSV
- HT Respond to < Anti HIV Cs / Thalidomide

---

① Traumatic: < Soft superficial Tender. d.t lack of Vaginal lubricant.

② Tuberculous < undermined Edge, pale Granuloc Floor → Post. scrotal (d.t extension From TB Epididymitis)

③ ♀ → ovae passed into urine & Faeces → Some deposited in the skin → Anogenital ulcers & Nodules.

4. Behcet. : → Recurrent < Genital ulcers / oral ulcers + ocular manifs + others [الكتب كلتيه عن Behcet]

5. H-Z → Multiple grouped vesicles on Erythematous base → ulcer [الكتب كلتيه عنه]
(Vulva, penis)

6. Mg ulcers → Bowen's & SCC of penis

1. old
2. uncircumcised under prepuce
3. ulcer
   - Edge → elevated / Everted
   - Floor → Hgic
   - Base → Indurated
4. Phimosis : in most cases → obscure the ulcer
5. 2ry bact. Inf. (gic)
6. Enlarged Inguinal L.N
   - either d/t < Cancer or Inf.

Diagnosis of Genital ulcers

Diagnostic clues

1. Traumatic → بتجيب منها حرقة بعد إلحاح
2. Behcet → oral + genital
3. Herpetic → مؤلم
4. H. Z → Dermatomal
5. Mg → غير مؤلم
   - Nodule plaque ulcer
   - Single
   - at Scrotum or penis
   - → Biopsy for SCC.
6. FDE: Recurrent at same time after intake of same drug.

Lab ....

(قاعدة)

No genital ulcer diagnosed without Lab. Invs.

1. ♂
   - DG → For
     - chancre → ulcer + ve multiple Bx
     - Not for Gumma
   - Serology
   - Biopsy → For Gumma.
2. Chancroid: Stained smear from G.T of ulcer → Gram's → Wright's
   - also Culture
   - Klebsiella granulomatis appears as clusters of blue organisms with chic "Safety Pin"
3. LGV: Culture from the ulcer → C. Trachomatis.
4. HSV2
   - Tzanck
   - Culture
   - IF
5. Mg: if suspected → Biopsy.

Balanitis

Def :. Inflammation of glans penis
. More common in unCircumCised
. prepuce is usually involved → "Balanoposthitis"

Predisposing Factors:

1. DM.
2. irritate by < Smegma / Urine alkalies / Ext. contacts
3. Trauma < Clothing Friction / long foreskin.
4. Pathogens < Venereal / Vaginal / Chlamydia / Viruses

Caused

A Infections Caused

B. Non Infections Caused

A Infections Caused

① Fungal: (Candidal)
. Commonest Cause
. there are 2 Forms < ... (See genital Candidiasis)

② Bacterial: May be d.t
Gram Cocci
i. Chlamydia
. in association with NGU
. Similar to that of Reiters

Mycoplasma: in ass. ē Mycoplasma NGU.

& balanitis (rare)

- Following chancre
- glans: whitish coalescent plaques on Edematous background.

Fournier's Gangrene: (Necrotizing Fascitis & ♂ genitalia,

- Cellulitis → Progress to → painful blue-brown Ecchym. discolor.
- Etiology: Bacteroids + G-ve bacilli
- predis. factors: DM
- ##: broad spectrum Antibiotics

Anaerobic Erosive balanitis:

Bacteroids
- G-ve bacilli
- Anaerobic
- Flora of GIT

B. Fragilis.

- d.f: Bacteroid.
- clp: Erosive gangrenous balanitis.
- ##: Flagyl

Group B beta Hemolytic Streptococci

- Commonest cause of Bact. balanitis
- Erythema & Edema of glans & C. sulcus. Coronal

③ Parasitic:

Amoebic Balanitis

d.f Entamoeba Histolytica

④ Protozoal.

Trichomonal Balanitis

30♂ & Men ē ↑ with or without Trichomonal

##: Flagyl.

Non Infectious Causes

1. Circinate Erosive Balanitis: See Reiters

2. Balanitis Xerotica Obliterans:

- LS ∇ genitalia
- C/P: Ivory-White, itchy, Macules on glans
  - phimosis may occurs (if prepuce affected)
  - Mg Transformation may occurs.

3. Zoon Balanitis (plasma cell balanitis):

- affect old or middle Aged uncircumcised
- Etiology: unknown but may be d.t reaction response to:
  - infection
  - irritation
  - injury

Considered as: "persistent Chr. idiopathic form of balanitis"

- C/P: Single or Multiple glistening plaque(s) of:
  - tiny erosion
  - Moist
  - Minute red specks (Cayenne pepper Sp.)
  - persists for Many Years
- pathology:
  - Dense band like infiltrate of Plasma Cells [lichenoid]
  - Capillary dilatation
  - Hemosiderin deposition
- (H) Cs, Gentamycin, Co2 laser, IL IFN α.

[4] Micaceous & Keratotic Pseudo epitheliomatous Balanitis :

Micaceous → start as Coronal balanitis → Silvery white appearance of mica like Crust → Nails,
+
Keratotic Hairy Masses on glans
with loss of prepuce Elasticity.

. Path: pseudoepitheliomatous Hyperplasia in reaction to infection.

[5] Other Causes

Ⓐ. FDE :
. lesion < Early : red oval or rounded swollen, ± blistering patches
Late : purpule - Brown Color
. Sites : Hand, / Feet & genitalia
. Drugs : may be: NSAIDs, Sulpha, Tetracycline
. onset : 30 mm - 8 hrs. after intake.

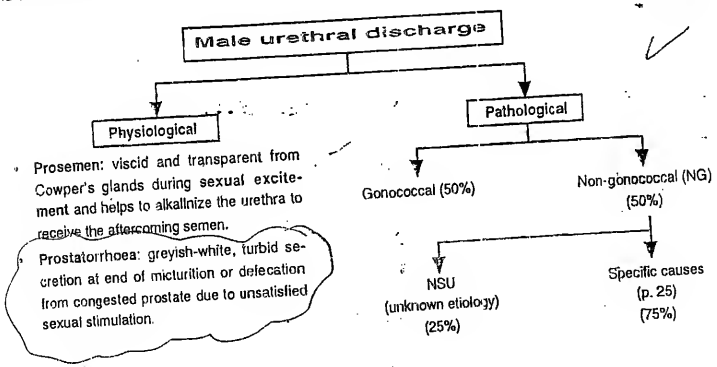
Ⓑ Dermatis
Ⓒ. Psoriasis
Ⓓ. L-P
Ⓔ. PIN (penile intraepith. Neoplasia). → Bowen dis
Ⓕ Scabies.

[#]: Acc. to the causes

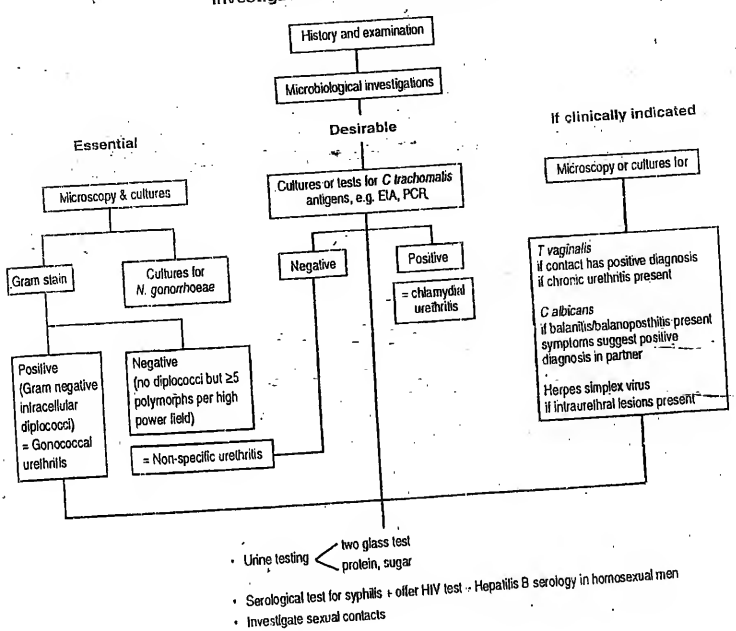
. Complications of Balanitis :
① phimosis.
② Mg

Male urethral discharge: Diagnosis

It is the commonest presenting symptom of STD in men.



Investigation of urethral discharge



Male urethral discharge

I) History

A) Of urethral discharge

1. **Site:**
   - Urethral infection
   - Subpreputial infection in uncircumcised men, e.g. herpetic or candidal.
2. **Quantity and color of discharge:**
   - Profuse yellow or green → gonorrhoea.
   - Scanty clear or white → NGU.
3. **Duration (IP)**
   - Gonorrhoea: 2-5 days.
   - Chlamydia or other types of NGU: 7-14 days.

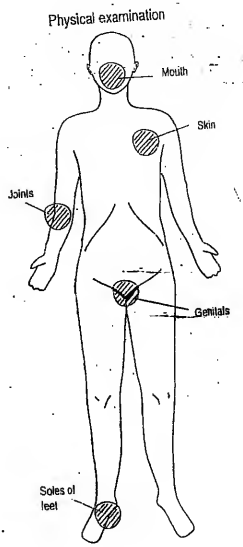
   NB: 5-10% of patients with G or NGU are asymptomatic.

B) Sexual history

1. **Number and type of sexual contacts** (homo- or heterosexual) in the previous 4 weeks.
2. **Homosexual:** which anatomical site(s) have been exposed to risk, e.g. rectum, throat, urethra or combination of all three.
3. **Sexual contact in other countries:** because of the development of resistant strains of N. gonorrhoea to penicillin in some countries.
4. **Number of partners and tracing of sexual contacts:** ? to determine the source of infection.

II) Examination

1. **Genitalia, pubic hair and perianal area.**
2. **General examination:** to exclude possible complications of G and NGU.
3. Examination of skin, soles of feet, mouth and joints.
4. A specimen of urethral discharge must be collected for Gram staining and microscopical examination for **Gram -ve intracellular diplococci.**
   - Present → Gonorrhoea
   - Absent + presence of ≥ 5 pus cells / HPF → NGU.
     - **C. trachomatis** cannot be identified by direct microscopy.
     - **T. vaginalis** (only in patients with chronic urethritis and in those whose female sexual contacts already have trichomoniasis). A specimen of discharge is placed on a slide (with one drop of saline), a coverslip added and examined without staining under microscope with dark ground illumination.



III) Culture

As up to 10% of cases of gonorrhoea may be missed if microscopy alone forms the basis of diagnosis, specimens of urethral discharge should be cultured for N. gonorrhoea.

IV) Confirmatory tests, serological tests and urine tests.

Management of urethritis "Urethral discharge"

- Men should be examined when they have not voided as long as 4 hours.
- Urethra should be stripped from posterior to anterior to detect urethral discharge if it is not present spontaneously.

I) Peripheral clinic without microscope

1. **Clinical differentiation between gonorrhoea** (= profuse, spontaneous yellow or green discharge) and NGU (= scanty discharge which must be expressed in order to be seen, clear or white as it contains fewer PMNLs). Patients fail to respond to penicillin for gonorrhoea may have penicillin-resistant gonorrhoea or NGU.

2. **Effective treatment for both conditions:**
   - Tetracycline 500 mg orally 4 times daily for 7 days, or better
   - Spectinomycin 2 g IM (single for gonorrhoea), followed by tetracycline 500 mg orally 4 times daily for 7 days for NGU.

II) Peripheral clinic with a microscope

- Confirm urethritis by presence of ≥ 5 pus cells in a stained smear of urethral contents. Examine smear for Gram -ve intracellular diplococci.
  - If Gram -ve intracellular diplococci are present → treatment of patient and sexual partner(s) for gonorrhoea.
  - If no such diplococci → treatment of patient and sexual partner(s) for NGU.
    1st choice: tetracycline 500 mg by mouth 4 times daily for 7 days.
    2nd choice: erythromycin (not estolate) 500 mg by mouth 4 times daily for 7 days, especially in pregnancy.

III) Intermediate Clinic

- Culture for *N. gonorrhoea*.

IV) Central laboratories

- Test for B. lactamase.
- Isolation and identification of *U. urealyticum*.
- Isolation, identification and serotyping of *C. trachomatis*.

Genital dermatoses

A. Itching

B. Pain

C. Infect°

D. lesions

A Genital Itching:

- pruritus Ani
- Balanitis
- pruritus Vulvae
- ECZema (AD, SD, CD, LSC & Intertrigo)
- others: PS, LP & LS.

B Genital pain:

- Balanitis
- Dyspareunia & Vaginismus
- Behcet-
- LP
- FDE
- Crohn's
- Pudendal Nerve entrapement Synd.
- Dysthesia
- others.
  - Reactive genital ulcer
  - Plasma Cell Vulvitis.
  - Atrophic – Vulvovaginit
  - Desquamative Vaginitis.

C. Infect° of Genital skin (♂ & ♀)

Sexually Transmitted

- ♀
- Gonorrhoea
- Chlamydial
- LGV
- Chancroid
- G.Inguinale
- TV, Chemoniasis
- Candidiasis
- others
  - H. genitalis
  - Genital Wart
  - Molluscum
  - Pubic louse & Scabies

Non-Sexually-Transmitted

(1) · Bact. : Boils, Impetigo, TB Erythrasma, BV

(2) · Viral : molluscum, Wart, HSV & HZ

(3) · Fungal : T. Cruris & Candidiasis

(4) Parasitic:
- Pubic lice & Scabies
- leishmaniasis
- Amebiasis
- Filariasis
- Schistosomiasis

D. Genital lesions

- Hidradenitis
- H:H
- Tm
  - PIN
  - VIN
  - SCC
  - Leiomyoma
  - EMPD
- PD
- Pearly penile papules
- Skalocystoma
- Nevi & melanoma
- Angiokeratoma
- Milia, epid. cysts
- Calcinosis

Complications of common genital infections

Complications		Infection		
		Gonococcal	Chlamydia Positive	Chlamydia Negative
Women				
• Local:	Pelvic inflammatory disease	+	+	+
	Bartholinitis / abscess	+	–	–
• Systemic:	Disseminated infection	+	–	–
Men				
• Local:	Epididymitis / orchitis	+	+	+
	Prostatitis (± vesiculitis)	+	+	+
• Systemic:	Reiter's disease	–	+	–
	Disseminated infection	+	–	–

Sexually transmitted arthritis

1. Disseminated gonococcal infection.
2. Reiter's syndrome.
3. Hepatitis B virus.
4. Lymphogranuloma venereum.
5. Syphilis of joints:
   a) Secondary syphilis: painless arthritis, tenosynovitis, bursitis or generalized painful arthralgia.
   b) Tertiary syphilis: arthralgia, synovitis or arthritis, bilateral bursitis of Verneuil, juxta-articular nodes.
   c) Late congenital syphilis:
      - Bilateral hydroarthrosis (Clutton's joint).
      - Von Gies joint.
      - True arthritis.
   d) Tabes dorsalis: Charcot's joint.
6. Others:
   - Mycoplasma hominis
   - Ureaplasma urealyticum
   - HSV
   - Epstein Barr virus
   - Cytomegalovirus
   - Chronic meningococcemia

	Chancre	Soft Sore
1. IP	9-90 days	3-5 days
2. No. of lesions	Single	Multiple, may be kissing ulcers
3. Pain	Painless	Painful
4. Edge	Sloping	Ragged undermined
5. Base	Firm, indurated	Soft
6. Bleeding	Does not bleed easily	Bleeds easily
7. Ooze	Serum	Seropus
8. Lymph nodes	Painless, discrete, firm, never suppurate	Tender, matted, suppurate & form sinuses
9. DG	+ ve	- ve
10. Treatment	Penicillin	Azithromycin, ceftriaxone

Mucocutaneous manifestations of HIV disease [1]

I) Infectious

1. Viral
   a) Herpes viruses
      - HSV
      - VZV
      - EBV → OHL
      - CMV
   b) HPV
   c) Molluscum contagiosum
2. Fungal
   a) Candidiasis
   b) Dermatophytosis
   c) Cryptococcosis
   d) Histoplasmosis
3. Bacterial
   a) Staph. aureus
   b) Atypical mycobact.
   c) Extrapulmonary TB
   d) Bacillary angiomatosis
4. Parasitic / protozoal
   a) Demodicidosis
   b) Scabies / phthirus pubis

II) Non-infectious

1. Papulosquamous
   a) Seb. dermatitis
   b) Psoriasis
   c) Reiter's dis.
   d) Xerosis / acquired ichthyosis
2. Folliculitis
   a) Eosinophilic
   b) Itchy
3. Drug reactions
4. Miscellaneous
   a) Vasculitides
   b) Pruritus
   c) Gingivitis / aphthosis
   d) Alopecias

III) Neoplastic

1. Epid. Kaposi's sarcoma
2. Lymphomas
3. Cervical cancers
4. Intraepithelial carcinoma

IV) STDs in HIV-infected patients

- HSV inf. differs in HIV Pts. than in Healthy in that
  - Clinically
    1. large irregular chr. Erosion or ulcerating
    2. disseminated lesions — Cut. systemic.
    3. Severe digital Inf.
    4. Herpetic Proctitis.

  (1 → genito-perineal, oral)

- Foscarnet: may be needed while others may be ineffective. why ??

- HZ: chr. / recurrent / Multidermatomal / disseminated
  - Cut. or
  - Visceral: CNS, RT, Liver

A large perineal ulceration(s) in a person with risk factors for HIV infection, should be considered HSV until proved otherwise.

3. EBV → Oral hairy leukoplakia (OHL)

- affect 50% of HIV pts after 5-10 yrs.
- also may affect any Immunosuppressed patients.
- Site → Ventrolat border of Tongue as asymptomatic / grayish-White, Corrugated, don't rub off.
- Prognosis: OHL — 48% → will develop HIV in 18m. / 80% → after 30 m.
- Tt = oral Acyclovir 400 X5 / Foscarnet.

4. CMV → "Opp" · Commonest virus Coinfect with HIV patient → Dissemination to many organs + Cut. / ulcers / vesiculobullous lesion. / vasculitis.

5. HPV
① ↑ Facial & intra-oral Warts
② difficult Tt of Condyloma Accuminata
③ CIN.

6. Molluscum < Wide spread Inf. / Giant Molluscum — "Opp" → Cidofovir.

Fungal Inf.

1. Candidiasis — Mucocut. is Very Common & Trachea, Oesoph, pharynx
   - Rx → Diflucan.
2. Dermatophytosis → Wide Spread Inf.
   - ① T. pedis → diffuse Hyperkeratotic
   - ② OM (Distal: الأظافر) (Proximal subungual) (PSO)
3. Disseminated — Histoplasmosis, Cryptococcosis, penicillinosis.

Bact. Inf. →

1. Staph → (Commonest).
2. MAC (MAIC) & extrapulm. TB.
3. &
4. Bacillary Angiomatosis → (BA) (Most)

def Bact. Inf. caused by G-ve bacilli

Genus Bartonella:

1. B. henselae: → Most cases of CSD & BA
2. B. Quintana — Some BA. Trench fever
3. B. bacilliformis → Bartonellosis (Includes Chr. Cut. lesions of Verruga Peruana)

• Clp 1. Hx. Contact with Infected Cat.
Transmission may be through < Scratching / Fleas

H: Cut / Systemic

2. Papules & Nodules < Single or Multiple (Hundreds)
red - violaceous vascular
simulating:
- PG
- Hemangioma
- Kaposi' sarcoma.

BA
Can affect Both
Immuno-Competent / Immuno-compromised.

3. Systemic spread → Liver, Spleen & Lung → Fever & wt loss.

• Histopathology → Stain: Warthin- Starry Silver

5 Ch
1. Epith. Collarettes
2. lobular proliferation of small BVs lined by < Large protuberant / cuboidal Cells.
3. Edematous Stroma
4. Leukocytic infiltrate & Lucocytoclastic debris.
5. Granular clumps of purplish material (Clusters of Bacteria)

Tx → 1. Erythromycin 500 x 4 /d.
2. Doxy.

BA Associated diseases

CSD

- Bg. & self limiting
- Qol → History of CS: ...
- Commonest cause of Bg > Chr. Adenopathy in < Children / Adults

CIP: Cut + L.N + Systemic

- Cut: Papule, Pustule or Nodule at hand & arm → ulceration
- L.N: unilat. Enlarged. Tender
- Systemic: .FAHM .HSM .CNS .Pneumonitis

path → ...

Bartonellosis (Carrion's dis)

AET: B. Bacilliformis.

CIP: 2 phases

Oroya Fever (Acute Endemic phase)

- In Non Immuned
- 100% of RBCs are Parasitized → Hemolytic anemia, Macrocytic Hypoch. an., RES infilt., L.N
- High MR d.t: anemia, septicemia, reactivation of TB.

Verruga Peruana

- In Partially Immuned
- 2ms after the Febrile stage.
- lesions: Maculopapular Erythem. in Extensors + Face. / Soft Hemangiomatous S.C Nodules.

Tt: 1. PCN 2. Streptomycin 3. Tetracycline 4. Chloramphenicol (IV)

Parasitic & Protozoal Inf.

① Demodicosis:

Demodex Folliculorum → itchy Follicular, scaly erythematous papules < Face / Head / Neck (Pityriasis follicularum)

- HH → Antiscabietic
  - Ivermectin
  - Permethrine
  - Crotamiton
  - Sulfur.
  - Metronidazole.

② Scabies

- either < classical or crusted
- DD From Ps & SD by — Hyperkeratosis, Crusting, Fissuring, Nail dystrophy.
- HH → Keratolytics + Antiscabietic.

Non Infectious Manifs.

[SD Xerosis [Ps Reiters (Follicular) DE

"Eczema"

① SD

Most common cut. manifs.
Frequently its the First diagnostic clue.
Clp → as usuall SD.
Path. → differs From SD in NL Individual in: Dermatitis Interface React°.
HH → as usuall SD

② PS
- if occur Before HIV → Worsening ← widespread pustular Erythrodermic.
- if develop after HIV Seroconversion → become nor. ← Palmoplanter Flexural Narl Arthritis.

HH
- Topical HH: as usual
- phototherapy: Care ē it as it may aggravate KS.
- Systemic HH:
  - MTX → leucopenia.
  - Cyclosporine & etretinate → good ē out CD4 affected
  - Zidovudine → marked improvement.

③ Reiter's → more severe in HIV.

④ Xerosis → generalized pruritus.
↓
d.t Malabs & diarrhea.

Folliculitis

Eosinophilic Folliculitis (EF)
- occur in advanced cases (CD4 < 200)
- follicular urticarial papules:
  - Severely itchy
  - Coalesce into → plaques ē papulovesicular border
  - at: Head, neck, upper back & upper arms.

Pruritic Papular Eruption (PPE) of HIV (Itchy Folliculitis)
Severely itchy red or skin colored papules on same distribution of EF.

Criteria for Ø & EF.

A Clinical Criteria:

- Follicular urticarial papules.
- Severely itchy
- distribution → [illegible]

B Histopathology: Eos < Infiltr. / Spongiosis / Abscess.

- Folliculocentric inflamm (Mainly Eos. but others ±)
- Follicular Spongiosis
- Eosinophilic follicular Abscesses.

C Lab Criteria:

- + ve HIV serology
- -ve invs for < Bact. / Fungi
- Peripheral Eosinophilia.
- ↑ Ig E
- CD4 < 200.

NB → PPE & EF → may be the same ds.

- Cut. Drug Eruptions: (d.t < altered Metabolism / ↑ basophil Reactivity).
  - Common in HIV patients specially Sulphonamides (> 50% of cases).

PV X 132

Mycoplasma Infections

deg. The smallest (125–250 nm) Free living microorganisms That lack The cell wall So < Not Stained by Gram / NOT Susceptible to beta lactams

They usually resides (NL Inhabitants) eg The Mucosa of < RT / GUT but never penetrate it Except If there is < Immunosuppression or Instrumentation → Invade the blood → dissemination To Many organs.

Need < Cholesterol / Urea for growth.

It has 3 Types:

1. Urea plasma Species < Urea plasma urealyticum, Urea plasma Parvum
2. M. Hominis
3. Other species < M. Genitalium, M. Penetrans

PPV

Diseases Caused by Mycoplasma < Genital: / Cutaneous:

U. Urealyticum Colonize: 5–20% ♂ 40–80% ♀

- Male: NGU, Epididymitis
- Female: PID, Bacterial Vaginosis (BV)
- Male & Female: may be followed by (RS)
- Infants: Fever, Pneumonia, RDS.

NB. Cut. diseases Caused by it:

- SJS
- EN
- Gianotti-Crosti Syd.
- Urticaria
- Morbilliform rash
- Acrocyanosis.

- U. Urealyticum → NGU & pneumonia
- M. hominis → Post partum fever
- M genitalium → Urethritis

Lab. Diagnosis

① Culture: Not indicated as routine Test but its main Indication is (persistent) NGU that's -ve for Chlamydia In order To do antimicrobial sensitivity Test To direct the tt.

Swab: Taken & Streaked on "Mycoplasma/Ureaplasma Selective" medium That Contain:
- agar base
- yeast
- horse Serum
- MgH Sulphate
- Urea / Ampicillin

Media
- Mycoplasma Media
- Sharts

↓ Incubate Anaerobically For 48 hrs at 37° C. | 10% CO_2 N_2

Needs
- N_2
- 10% CO_2
- 37 C

Fried Egg Colonies to differentiate bet the 2 →
- U. Urely: Small (Satellite) . brown Color . Color Change in media containing Urea
- M. Hominis: . large (bo-Sm) . Color Change in media Contain Arginine.

② ELISA & CFT:

Treatment ① Tetracycline: effective against < Chlamydia & Mycoplasma

② Erythromycin: as in Chlamydia.

③ AZithromycin

④ others
- clindamycin
- Levofloxacin & ofloxacin.

NB
- U. Urealyticum → ofen ↓ → Erythromyci-
- M. Hominis → Clindamycin effect is not other Species.

Chancroid

No Inguinal (Soft Sore - Soft Chancre, Ulcus Molle)

One of STDs caused by (G-ve ba cilli) "H. ducreyi" &

Ch^r By: . Acute genital ulceration
. Inguinal adenitis (buboes)
. NO systemic manifs.

. Epidemiology: Most painful ulcer

. Incidence → The Commonest cause of Genital ulcer in many developing (Poor) Countries.

. Age: ≃ 30 Yrs (age of Maximal sexual Activity)

. Sex: M : F = 10 : 1 (↑ if ← Uncircumcision / Heterosexuality / Promiscuous practice)

. organism: → (Haemophilus Ducreyi)

. G-ve bacilli (Facultative anerobes)
. Small size & Typical (chaining pattern)

Prostitutes → . Can survive only @ high Turn over of Sex partners → So unsuitable.
in areas of low rates of partner change

. Pathogenesis: organism inoculation occurs via Microscopic barrier defects in Epid. → Th1-mediated Inflamm. & → regional Adenitis.

CIP

IP : 3-7 days (or 8ds - 3 wks)

Start as : papule → pustule → ulcer.

The ulcer ch-b/:

No → usually multiple (may start single & d.t apposition → multiplicity & ± coalesce → Giant ulcer)

Kissing ulcer

Site : The commonest site in:

- Male
  - Foreskin (prepuce) < Ext or Int
  - others / sulcus / frenulum / Glans / shaft.
- Female
  - Labia Majora
  - other / L. minora / Thigh / Cx / perineum.

Size : 2mm - 2 Cm.

Shape : irregular or serpigenous.

Edge : undermined & ragged.

Floor : Covered by < GT. / Purulent Exudate.

Base : soft (Not Indurated).

Fixation : Not fixed.

Tenderness → +Ve. (Most painful genital lesion).

Discharge → purulent urethral discharge
In case ↑ urethral lesions.

- L.N / Tender, Fixed, matted → ulceration through skin → discharging sinuses & Fistulae.
  - usually Unilat.
  - +ve in 50% (♂ > ♀)
  - Skin
  - under-structures

→ • Pathognomonic signs for Diagnosis:

1. Genital ulcer < Multiple. / Soft / painful & Tender
2. Inguinal L.N < Tender / Suppurate (bubo). : usually Unilat.

→ • Criterial For Diagnosis:

1. 2 Clinical (Pathognomonic).
2. 2-Ve Invs < dark ground Mic. & Serology for ♂ / Tests for HSV.

• Diagnosis:

1. stained smear: Swab from the ulcer will show G-ve Extracellular Coccobacilli in many patterns:
   - Single.
   - Clusters
   - Schools of Fish
   - rail road Tracks
   - Fingerprints.

   "Chain pattern" → usually Extra-Cellular PMNL

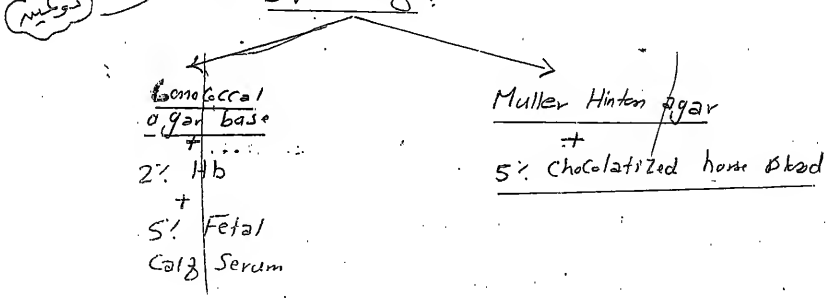
   - disadv / Non Sensitive / Specific (many other bacteria may similar to it & many specimens don't show the organism

② Culture:

. The accepted standard for D. (60-80% Sensitivity).

. Media: Nairobi Media consists of

Biplate of:



③ PCR: . replace the culture in many Centers.

. good on samples prepared from H. ducreyi culture.

. less sensitive when used to test genital ulcer specimen.

④ Multiplex PCR: (Simultaneous amplification of DNA Targets from H.ducreyi & organisms)

. تشخيص ulcer في نفس العينة HSV H.Ducreyi

⑤ Monoclonal Antibody: detect H. Ducreyi on ulcer specimen.

⑥ Serology: Not useful.

⑦ Pathology → Not recommended for D.; only for Excluding Malignancy in Non Healing lesions

⑧ Tests for D of other STDs: S & HIV

3 Zones:

- Peripheral: Neut. + fibrin + RBCs + Necrosis
- Mid: Neo Blood V. + endothelial cell prolif → occlusion → Thrombosis
- Central: dense plasma cells & Lymphoid Cells.

(Typical of D)

DD → Genital ulcer (Sp. ?)

Tt
- AZithromycin → 1gm Single dose
- Ceftriaxon → 250 mg Single IM dose.
- Ciprofloxacin → 500 mg x 2 x 3.
- Erythromycin base → 500 mg x 4 x 7

also
- Sulfa
- ~~Steroids~~

NB
- The partner from 10 ds preceding the onset of symptoms should be examined & tt triggered.
- patients with chancroid + HIV → same tt regimen but with more prolonged period.

NB: Chancroid & HIV:
- Incid. of HIV Inf. & Transmission is markedly ↑ in presence of Genital ulcer
- Genital lesions therefore become both: ① a portal of Entry for non infected Individuals ② Exit for already HIV infected persons.
- In H. ducreyi ulcer: There is ↑↑ No of Macrophages & CD4, both ↑↑ Expression of Chemokine receptors < CCR5 & CXCR4 These are 2 main Co-receptors essential for HIV entry.
- RANTES Chemokine: ligand for CCR5 → present in papular & pustular Stages of d/s.

NB
- CCR5 & CXCR4: belong to Class 7 Transmembrane G-protein Coupled receptors.

Granuloma Inguinale = Donovanosis
(Granuloma Venereum)

- **def:** rare chr. progressive ulcerative bacterial Infect° caused by Calymmatobacterium (Klebsiella) granulomatis (G-Ve)
- **Causative organism:** Klebsiella granulomatis ; G-ve bacilli.
- **Mode of Transmission** < STDs / Vertical (via infected birth canal) / Fecal contaminat°
- **Pathogenesis:** ✗
  - **The 1ry lesion:** Small Cut < Papule or Nodule contains Mononuclear cells & Cytoplasmic Vacuoles Filled with microorganisms (ϖ will rupture → release of "Donovan bodies"

C/P (IP: 9 - 90 d).

Genital lesions:

Papule or nodule ch By:

- Red Painless → Erodes Beefy granulomatous ulcer & rolled edges (Painless genital ulcer) (GU)
- **L.N:** Not affected Except if:
  - 2ry bact. Inf. or
  - Extension of inflamm. to it.

Ulcer:
- Beefy
- painless
- Granulomatous
- Edge: raised rolled

- **If untreated:** lesion may remain dormant or progress slowly involving whole of Ext. genitalia, anus, Inguinal Area.
- **Healing:** ∴ Severe fibrosis & tissue destruct°.

Extragenital lesions:

± d.t.: either Autoinoculat° or 2ry To dissemination

site:
- Commonest → Bone
- others → Skin, Intra-abdominal cavity & oral cavity.

Site of genital lesions

- Male
  - prepuce
  - glans
  - frenulum
  - Coronal sulcus
- Female
  - Commonest is Vulva

"Inf. Ago"

NO L.N (Except if 2ry bact. Inf.

. Clinical Varieties:

① Ulcero Vegetative (most Common):

. arise from The nodular Type

. ulcers or By (large, spreading, painless, Exuberant)

② Beefy red & bleed easily

③ Edge → raised rolled

④ Base → clean friable.

② Nodular Type (See before): may be similar to LGV (Pseudobubo)

③ Cicatricial Type: Dry ulcers evolve into cicatricial plaques & may be ass. with Lymphoedema.

④ Hypertrophic or Verrucous.

E = Wart-like nodular type

↓

In later stages of the dis → Elephantiasis

Diagnosis (Stained smear – Culture – PCR – Serology – Pathology &..)

1. **Stained smear:** From Tissue scrapings stained with ⟨Giemsa / Wright / leishman⟩ stain → **Donovan Bodies**.
   - Vacuoles containing bacilli ē in Macrophages. or PMNL.
   - **Morphology** ⟨Coccoid / Coccobacillary / Bacillary⟩
   - **Staining:** → Bipolar staining present at 2 ends of the organism → "Safety pin" appearance

2. **Culture** → difficult; Can be done on ⟨Human peripheral blood Mononuclear Cells. / Hep 2 cells.⟩
   - No Arthropod media.

3. **Histopathology:** (Also to Exclude Carcinoma)
   (Biopsy & Tissue Crush Preparation): → Safety pin appearance
   Biopsy or scrap from ulcer Edge
   ↓
   Crushed bet. 2 glass slides
   ↓
   Separated, air dryed & Stained
   ↓
   Safety pin appearance of Donovan Bodies

4. **PCR** (under trial)

5. **Serology** → Not useful.

Complications

- Urethral Stricture & elephantiasis
- Rectovesical Fistulae in ♂
- Elephantiasis of genitalia & L.L
- Superinf. by Fusiform bacilli → Phagedenic ulcer.
- SCC.

Treatment

(٣ أسابيع)

1. TMP & SMX + Doxy 100 X1X2
2. Azithromycin
3. Cipro 750 X2/d + Erythromycin 500X4/d
4. Norfloxacin.

ماجستير تناسليه (3)

S.T.D

د/هانى ابوالوفا

2017

د. مسلم

just print

01025329200- 0502200362

HIV disease (AIDS)

0/00 / 2313616

def: HIV dis. disease ch. by defective cell mediated Immunity occuring in persons with no cause of Immunodeficiency other than HIV.

While AIDs: Severe end stage of HIV dis. ch. by (3) { CD4 < 200 / opportunistic Inf. / Mg.

History of Epidemics

origin: From non Human primates in Sub-Saharan Africa & Transferred to humans by direct contact during Hunting or butchery.

(جنوب الصحراء)
Subsharan Africa
جنوب الصحراء الكبرى
جنوب أفريقيا
بتسراا
زيمبابوي

Luc Montagnier et al.

History of the epidemic	
1981	Cases of pneumocystis carinii pneumonia and Kaposi's sarcoma in the United States.
1983	Discovery of the virus.
1984	Development of antibody test.
1993	CDC definition of AIDS: all those with confirmed HIV infection + CD4 count <200/mm³ ± indicator dis.

Table 22.3: Nomenclature of AIDS virus

1983	:	Lymphadenopathy associated virus (LAV)
1984	:	Human T-lymphotropic virus type 3 (HTLV-3)
	:	AIDS related virus (ARV)
1986	:	Human immunodeficiency virus (HIV)
1987	:	HIV-1 and HIV-2

Zalcitabine
1-5 mg/kg
PN
pene
C/T ulce

HIV Virology
- Class
- Ch
- Structure
- replicat cycle
- Types.
- Epidemiology
- Trasmission.

Class:

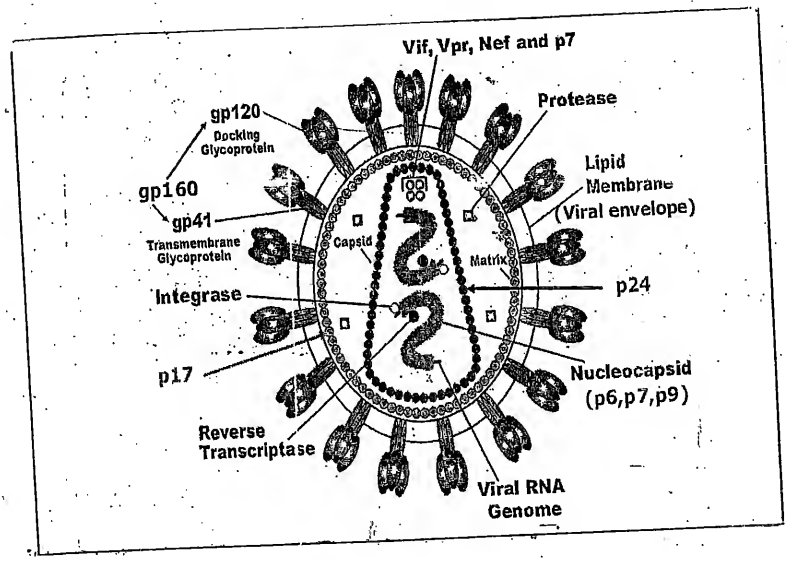
Genus: Lentivirus

Family: Retrovirus (Retroviridae = Contain Enz. Reverse Transcriptase)

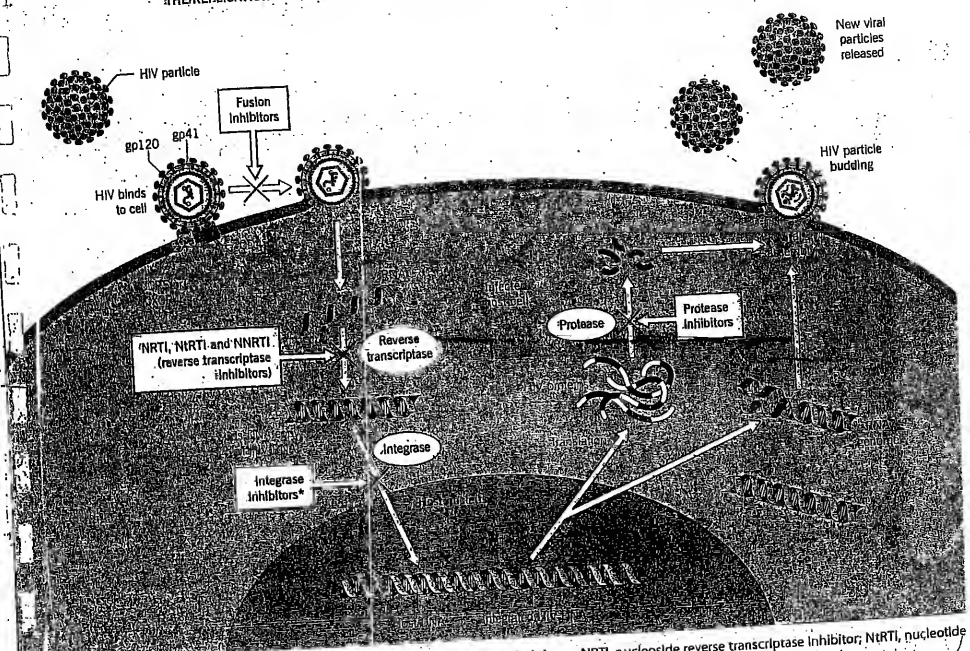
- General Characters:

RNA virus (Contain 2 single RNA Strands)

Contain (2) Reverse Transcriptase Enz. (Can make "Transcribe" DNA Copies from its RNA inside the Host Cells in a Retrodirection)



THE REPLICATION OF HIV WITHIN CD4+ LYMPHOCYTE AND TARGET SITES OF ANTIRETROVIRAL DRUGS



7.2 Replication of HIV within CD4+ lymphocyte and target sites of antiretroviral drugs. NRTI, nucleoside reverse transcriptase inhibitor; NtRTI, nucleotide
rse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor. *Drugs are currently under development.

3. Latency
4. Persistent Viremia
5. Nervous System Inf.
6. weak host immune responses
7. High affinity For CD4 Tcells & Monocytes.

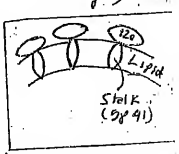
Structure

A Molecular structure: (3 p.)

1. 2 Envelopes ← lipid. Glycoprotein

- Inner lipid (bilayer) Envelope → derived from the Host cells.
- outer Glycoprotein (gp) Envelope (spiked Envelope)

This spike has 2 parts.



- outer (Cap) — Called: gp 120 (in Both HIV1 & 2)
- Inner (Stem = stalk) → Penetrates the lipid envelop

In:
- HIV1 Called: gp 41
- HIV2 Called: gp 36

NB: The protein envelope allows attachement & Fusion with Target cells. (gp120 & 41)

2. Capsid: [(viral)

" Conical shapped protein shell Called (P24) (enclose genetic material).

Surrounded by a matrix Protein Called: (P17) (Ensuring Integrity of the Virion)

(3) 2 RNA Copies (2 Single Strands):

↓

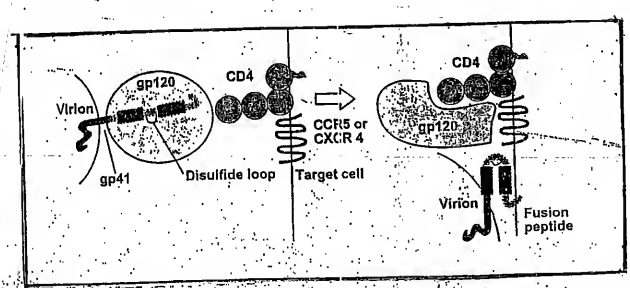
Tightly bound to:

Nucleocapsid Proteins	Enzymes (RIP)
· P6	· Reverse Transcriptase.
· P7	· Integrase
· P9	· Protease.

Pathophysiology of HIV infection (Replication Cycle):

- Types of Targeted Cells:
  1. CD4+ T Cells
  2. Macrophages
  3. Dendritic Cells
  4. Microglial "

HIV disease is the most common cause of death among the infectious diseases.



H.I.V. • Viral Replication Cycle

1. viral entry → attachment (Binding). / Fusion / uncoating & Entry
2. provirus formation
3. provirus Integration
4. Transcription & Translation
5. viral Assembly
6. viral budding.

Viral Entry

1. **Attachment (Binding)**: Attachment of viral proteins gp120 & gp41 to Target Cell receptors CD4 & CoReceptors < CCR5 or CXCR4

2. **Fusion**: bet. the viral Envelope & ! Host-Cell memb. (d.t penetrate of CM by gp41 → Approximation of 2 CMs → Fusion).

3. **uncoating & Entry**: Virus is uncoated (as) it penetrate The cell → release its genomic material Into Host Cell Cytoplasm. & Leave it < gp120 / gp41 on Host Cell surface. (CD4)

genomic material — gp<

Provirus Formation

The enz. reverse Transcriptase makes viral DNA (provirus) From The viral RNA.

(ss RNA ——→ ds DNA)

Provirus Integrase

The provirus enters the nucleus & become Integrated to the Host DNA by the enz. "Integrase"

Transcription & Translation

. Transcription of provirus DNA Into RNA.

- Formation of the Genome of the New viral particle
- "Translation" into viral proteins (mRNA)
  - "Protease enz." (Protein Progeny before Assemb)
    - Cleavage into the structural components of the virus. (e.g gp160 precursor → gp120/41)

Viral Assembly

. the genomic RNA + viral proteins (enzs) → Assembled to Form intact Virions. (virus)

Viral Budding

Intact virus is released by "budding" from the infected cells. (taking lipid Envelope from the Host Cells).

Marked Viral Mutate
Marked ↓ CD4 +.

Cellular death (CD4) Mechanism

① Newly formed virus ē gp120 spikes → bind to adjacent CD4 → make holes → swelling & death.

② The Host cells will surface proteins gp 120/41 will:
- recognized as foreign Ag → CD8 attack it → death.
- Adhere to adjacent CD4 → Syncytium Formation (≈12 dozen)
  → Syncytial cell death.

Syncytium: Giant or large cell like structure

↓

after marked depletion of CD4+ Macrophages become the Source of HIV production.

Types of HIV

HIV1	HIV2
• originated From "Chamanzee"	• originated From "Sooty Mangabey" → سعال، زكام
• World wide	• Mainly West Africa
• More virulent	• less virulent
• Easily Transmitted	• less transmissable.
gp41 & VPU gene	gp36 & VPX gene

HIV1 Subtypes

(From A-G: Acc. to Geographic distribution)

Area	HIV1 subtype	Spread	Epidemiologic data
شمال امريكا جنوب اوربا استراليا	B	. Homosexuals . Bisexuals . IVD abusers	. M:F (10:1) . rare in Infants
جنوب افريقيا الكبرى آسيا آسيا	ACD C B E	→ Heterosexuals . as ↑ + IVDAs . as ↑	All . M:F = 1:1 . Common infant infect.

Epidemiology of HIV Inf: (2007):

(i) Pandemic began on (1981)

(ii) 40 million of world's population is infected → 25 millions deaths.

By HIV

- > 90% Infect in developing Countries
- > 5 million في جنوب افريقيا

2005
- ١٤٠٠٠ حالة ايدز
- ٥ ملايين = حالة HIV
- ٣ مليون حالة وفاة

• اكثر بقاع انتشاراً:

(Subsaharan Africa) → . AFrica → 68.5% (25 million)
. Asia → 14.5%
. High income Countries → 6.5%
. Latin America → 5.5%
. Eastern Europe → 4.5%

. Since 1981 → 25 million deaths.

- Mode of Transmission:

① Sex: (70-80%) : (Commonest Mode)

- Vaginal (60-70%): Major route of spread in Africa
- Anal (5-10%): → Major route of Transmission in Europe & USA
  - The presence of Mucosal Trauma & Genital ulceration → Facilitate the spread.

"Risk" ↑ with: Genital ulcers & HIV inf. ?? (See ⑤)

- Oral: → Very rare.

② Contaminated needles (5-10%) ← Inj. / Accid. (<0.01%)

- IVD Abs (IV drug Abusers).
- sharing needles.
- Injections.

③ Transfusion of Blood & Blood products specially in hemophilics.

④ Mother to child Transmission: (MTC) (5-10%):

- Intrapartum (Commonest): through Contact with cervical & vaginal secretion.
- Antepartum → Transplacental: (In utero).
- Breast feeding.

⑤ Organ & Tissue Transplantation & donation: eg

- Skin
- Kidney
- Corneas
- semen
- BM
- Tendons

⑥ Accidental: among Health care workers: is extremely rare (<0.01%) as Needle prick injury

NB ① HIV: has been Isolated From all body Secretions as:

- semen
- Cervical secretions
- CSF
- Tears
- urine
- saliva
- Lymphocyte
- Plasma

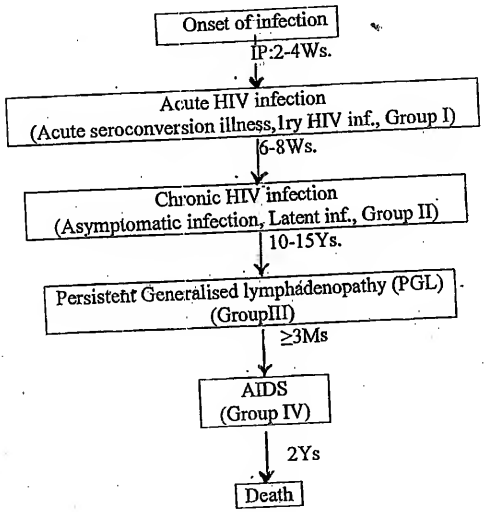
↓

- & this doesn't mean that all can Transmit the Inf because Concentration & virus in them varies Considerably
- the most Infectious of them: (اكيد تركيز)
  - Blood
  - Semen
  - Cervical Secretions

② There is No Evidence That: the virus is Transmitted By Casual or Social Contact: e.g

- Mosquitos
- Swimming pools
- Cups
- Toilets
- Air Space

C/P of HIV inf.: Natural History:



So C/P of HIV inf.
(عبارة عن ٤ مراحل)

1) Acute HIV infection
(Acute seroconversion illness,1ry HIV inf., Group I)

- Def. period between Exposure to the virus & full development of Antiviral Antibodies = (window phase) (when antibody test becomes +ve for HIV)
- onset: 2-4 ws after inf. (IP of HIV)
- durat°: 6-8 ws.
- Manifs: Asymptomatic in ≃ 30%
  Symptomatic ≃ 70% → Non specific (Influenza like manifestations):
  1. General: FAHM & L.N (Generalized)
  2. Hematological: Anemia & thrombocytopenia.

(3) Neurological < Neuropathy.
Myelopathy.

(4) Dermatological: < maculopapular rash at trunk
Reactivation of Shingles: (Indicate Modest ↓ in Immunity).

(5) Mucosal:
"ثرش" Thrush d.t Candida (Sign & Marked ↓↓ in Immunity ---> (CD4 200-500 Cells/UL)

- Oral Hairy leukoplakia: (Vertical white plaques at side of tongue Can't be rubbed off.) (Hairy like with Hyperkeratosis)
- HSV inf. (d.t EBV) → Other Causes < Behcet, Ulcerative Colitis, HIV + Smoking.
- Aphthous ulcers & Post. Oropharynx.

- Events: أحداث تحدث
- Viral load → Peak ↑↑ (Most Sensitive For ⚠) ثم تقل تدريجيا
- CD4 Count → Peak ↓↓ ثم تزيد تدريجيا.
- P24 Ag → +ve (تظهر في فترة الشباك ...)
- Antibodies < Anti P24, Anti gP41 → -ve (Window phase)

CIP ثبت

Definition
Onset
Duration
Manifestations
Events:
-Viral load
- CD4 count
- P24 Ag
- Antibodies(Anti p24 and gp41)

تأكيد التشخيص

لإجراء فحص عكسي بن

- Viral load & CD4 count.
- P24 & Anti P24

(2) Chronic HIV infection (Asymptomatic infection, Latent inf., Group II)

- **Onset:** With full development of Antiviral Antibodies (after Termination of Acute Sero Conversion illness).
- **duration:** 10–15 Ys. (then → AIDs)
- **manifestations:** → Asymptomatic but some patients having persistent Generalized L.N (PGL)
- **Events:**
  - **Viral loads:** ↓↓ [to its lowest point (Viral set point) & persist at relatively steady state] d.t effecient Immunity (Abs)
  - **CD4 Count:** Progressive ↓↓ (50 cells/year) → steady
  - ✓ **P24 Ag:** - ve
  - ✓ **Antibodies** < Anti P24 → +Ve ; Anti GP41 → +Ve (once +ve → always +ve)

] ← signs

(3) Persistent Generalised lymphadenopathy (PGL) (Group III)

- **onset:** during the Asympt. stage. (it affects some pts)
- **durat°:** till onset of AIDs (≥ 3 m)
- **Manifs:** Generalised L.N that's ch By's
  - → . L.N > 1Cm in diameter
  - → . ≥ 2 Extrainguinal sites
  - → . ≥ 3 m, durat°
  - → . Not d.t Any other Cause.
- **Events:** . viral load, CD4 & Antigp 41 → as Asympt. inf.
  - ✓ P24 → start to be +ve
  - ✓ Anti P24 → " " " - ve

[Bad Prognosis] AIDs قريب

PGL

- May be the presenting Feature of HIV
- may be clue that the patient will progress to AIDS

4- AIDS (Group IV)

- **Definition:** End stage of HIV disease that is Ch. By Δ:
  - CD4 < 200
  - opportunistic Inf.
  - Malignancy.
- **onset:** 10-15 yrs from onset of Inf.
- **durat:** ≃ 2 yrs (then death).
- **Manifestations:**

(A) **General Manifs:** < ARC. / HIV Encephalopathy

ARC = Chr. Fatigue Synd. = HIV wasting Synd.

(I) **Constitutional Manifs.** (AIDs related Complex = Chr. Fatigue syndrome) [ARC]:

mild prodromal manifs. in HIV patient That may precede the appearance of Full-blown AIDs & its Serious Manifs.

- **Diagnosis of ARC,** (≥ 2 clinical + ≥ 2 lab).

1) **Clinical:**
- Fever ≥ 38 °c
- diarrhoea
- w.t loss ≥ 10% of BSA
- Skin Rash (Maculopap).
- HZ (Multidermatomal)
- OHL. oral Hairy leukoplakia
- oropharyngeal candidiasis.

2) **Lab.**
- CD4 < 400 (in AIDs < 200)
- ↑ Igs (in " → ↓↓)
- Follicular or mixed Hyperplasia of L.N (in AIDs ↓ degen.)

- **Causes of Death in AIDS**
  1. Opportunistic Inf.
  2. Wasting
  3. Encephalopathy
  4. Mg (less common)

(II) **Neurologic dis.** (HIV encephalopathy)

If / Untreated HIV → Oral Candidiasis (Thrush) → AIDs in 6-12 ms.
\ OHL

العدوى المنزعة إلى تكليف تقرى ان المريض في طريقه لـ (AIDs) بعد ... "حتى"

(A) Opportunistic Inf.: (AIDs)

1. Bacterial:
   - Mycobact:
     - TB (Extrapulm.).
     - Atypical Mycob. → MAIC (M. Kansasii (disseminated))
   - Salmonella: Recurrent bacteremia.

2. Viral:
   - HSV: chr. mucocut. (>1m) or disseminated.
   - VZV: Recurrent, Multidermatomal.
   - EBV: OHL
   - CMV: infect:
   - PML: Progressive multifocal leukoencephalopathy. [Fetal viral dis CH BY progressive damage of White Matter of brain]

   John cunningham Virus → JC Virus

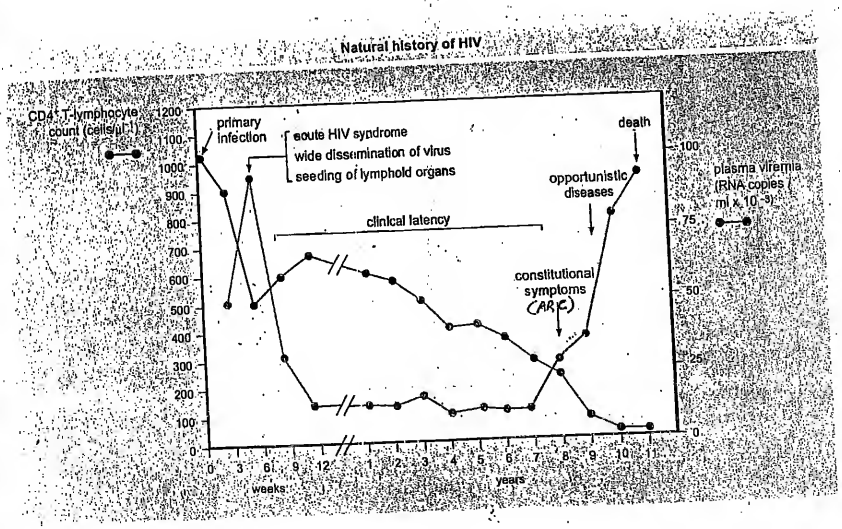
3. Fungal: (CCH)
   - Candidiasis (Thrush): Esophagus, Trachea & bronchi.
   - Cryptococcosis: (Extrapulm.).
   - Histoplasmosis: (disseminated).

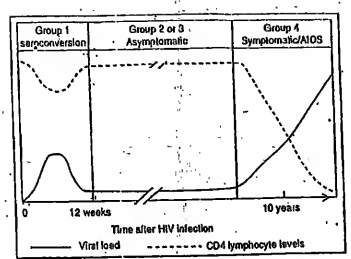
4. Parasitic: Strongyloidiasis (Extra intestinal)

5. Protozoal:
   - Pneumocystis Carinii Pneumonia.
   - Cryptosporidiosis (& Chr. diarrhea >1m)
   - Toxoplasmosis of Brain.

(B) Malignancies:
- Kapasi sarcoma.
- Lymphoma (non Hodgkins & dry lymphoma of the brain).

Events:
- Viral load: Very High ↑↑
- CD4+ Count: Very low ↓↓ < 200
- P24 Ag → +ve
- Antibodies: Anti P24 → −ve; Anti gp41 → +ve





Association between virological, immunological & clinical events & time course of HIV infection

· CDC Classification (Staging) of HIV

(1.) CDC 1992 :

Table 22.6: CDC classification of HIV disease (1992)

Group I	:	Primary HIV Infection (Acute Sero Conversion)
Group II	:	Asymptomatic Infection (Latency)
Group III	:	Generalised lymphadenopathy (PGL)
Group IV	:	AIDS
Subgroup A	:	Constitutional disease (ARC) & HIV wasting Synd. (Slim)
Subgroup B	:	Neurologic disease (HIV Encephalopathy)
Subgroup C	:	Secondary infectious disease (opportunistic inf.)
Subgroup D	:	Secondary Cancers
		Kaposi's sarcoma
		Non-Hodgkins lymphoma
		Primary lymphoma of the brain
Subgroup E	:	Others :

(2) CDC 1993 :

CDC 1993 classification system for HIV disease

	(1)	(2)	(3)
CD4 lymphocyte count x10⁶/l	>500	200-499	<199
(A) Asymptomatic including groups I, II and III	A1	A2	A3
(B) Symptomatic (Not A or C)	B1	B2	B3
(C) AIDS-defining conditions	C1	C2	C3

- dis. d.t severe or Complicated BY HIV inf.

Opportunistic Inf.

(A) = Asymptomatic

(B) = Symptomatic = diarrhea, fever, Candida, ...
(Not manifs. of seroconv. or AIDs)

(C) = AIDs: A3, B3, C1, C2, C3.

Laboratory Dx of HIV

1. Viral Load
2. Viral Culture
3. Viral Antigen
4. Antiviral Antibodies
5. others.

1. Viral load Assesment:

Methods: 1. RT-PCR test (Reverse transcriptase PCR)
2. b.DNA test (branched DNA).
3. NASBA (Nucleic acid sequence based Assay).

Advantage

1. Diagnosis of: Early Inf. / Late Inf.

Highly sensitive detect even non Replicating virus.

A. Early Inf.: during window phase (it is window phase to ≃ 12 d)

B. Infants ē HIV mother.

C. Late Inf.: when There is False -ve ELISA & WB (d.t Severe Immunodeficiency

Antibodies (False -ve)

Very

2. Assessment of dis. progression (Viral load)

- Acute seroConversion → ↑ load
- Asymptomatic inf → ↓ load (set point) in 6 ms of inf.
- (AIDs). Symptomatic inf. → ↑ Load.

③ Assesment of HH Efficacy:

if with HH HIV RNA

↓↓ in 1w → Good response

↑↑ → emergency drug resistance.

30-100 Fold ↓ in viral load.

- disadv: ① sensitive but non specific.
② Net Yet standarized.

↓

⑤ Not used as a diagnostic tool.

2 Viral Culture:

- Source (HIV): peripheral Blood lymphocyte (PBL), CSF, TISSUES
- Adv. → Most specific (ultimate diagnosis)
- disadv: → • difficult
• Expensive
• Not for routine use.

3 Viral Antigens (P24 detection):

- Method: Monoclonal Antibody
- Value: ① Diagnosis: → early diagnosis of Inf. before Anti Viral Antibs. (seroconversion illness).

② prognosis: → reappearance after its disappearance → Bad Prognosis (Late Inf.)

③ Assessment of HH Efficacy

P24 Ag

- Abs في الدم (Early Inf) → +ve
- Abs في الخلايا (GII) → -ve
- Late Inf (GIII & IV) → +ve → poor prognosis

disadv. (1) low sensitivity (Fluctuat نتائج)
(2) Not yet standardized.

في البداية بنستعمل (HIV RNA PCR)

4 **Antiviral Antibodies:**

- 3 Abs: Anti < p24, gp41, gp120/160
- 3 detection technique: ELISA, WB, RIPA.

لازم تفهم كده ← **Fluctuation (physiology of Anti HIV):**

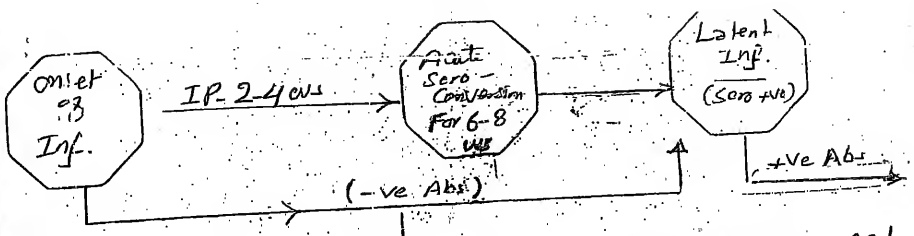
(1) Onset & appearance: Immediately after Inf. & during Acute seroconversion illness the Antibodies can't be detected & this period of -ve Antibs called "Window phase" (3 ms – 6 ms)

So Antibody Tests are (False -ve)

- usually: 3 ms Then sero +ve
- Most cases (95%) → are sero +ve at 6 ms
- 12 ms window phase: may occur in HIV in ART or HCV.

(2) once they are +ve, Anti < gp41 → remains +ve; p24 → remains +ve Except at PGL & AIDS they are (-ve)

- Sero Assessment BY
  - ELISA → always +ve because it detect both anti (p24, gp41) together even in PGL & AIDS.
  - WB for
    - anti gp41 → remains +ve.
    - anti p24 → become -ve at PGL & AIDS.



Window phase = IP + duration of Acute illness = 8-12 wks (غالبا ٣ شهور)

-ve Abs

A ELISA

- detect Antibodies Against The whole viral proteins (P24, gp41 & gp120)
- Ch by (1) Sensitive (Good -ve Test)
  (2) Non Specific (False +ve)

عشان كده once +ve → always +ve.

Eg. So it is: The most widely test used for screening of Blood donors.

NB. False +ve in:
- Blood Mg
- MM
- BPC
- DNA viral inf. (HCV).

HIV + HCV (كده)

B Western Blot

(Abs ضد نوع واحد بس من Viral Proteins)

- detect Antibodies against certain single specific viral protein (purified HIV proteins used as:
  - P24
  - gp41
  - gp120/160

عشان كده

- Specific (Confirm & Rules out false +ve ELISA)

WB
- gp41 → once +ve always +ve
- P24 → Fast → +ve, Late → -ve (PGL & AIDS)

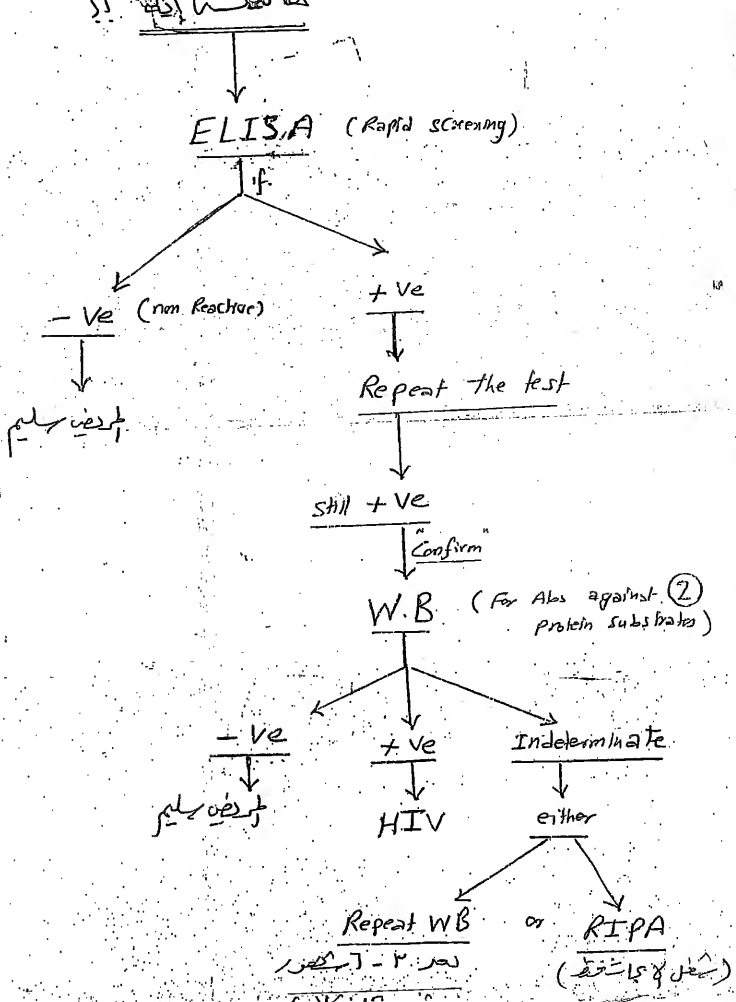
لازم عشان نقول انه إيجابي يكون فيه Abs ضد نوعين من البروتينات (مش نوع واحد بس)

C RIPA

- Radio Immunoprecipitation Assay.
- Adv: clarify atypical or Indeterminate WB
- disadv: Not yet standarized.

لو جالك مريض (أو عينة دم) وشاكك أنه (HIV) هتعمل إيه؟؟

سؤال شفوي في



5 → Other Investigations : (see the table)

Table 22.11: Other tests to be performed in AIDS

1. Hemoglobin concentration
2. Total-and differential leukocyte counts
3. Quantitation of CD4 and CD8 lymphocytes
4. Platelet counts
5. Serologic tests for syphilis
6. β-microglobulin level
7. Hepatitis B and toxoplasma serology
8. Skin tests for tuberculosis and one or more control antigens
9. Skiagram of the chest

Tuberculin

NB : . Total Leucocytic Count : 4000 – 11000 /mm³

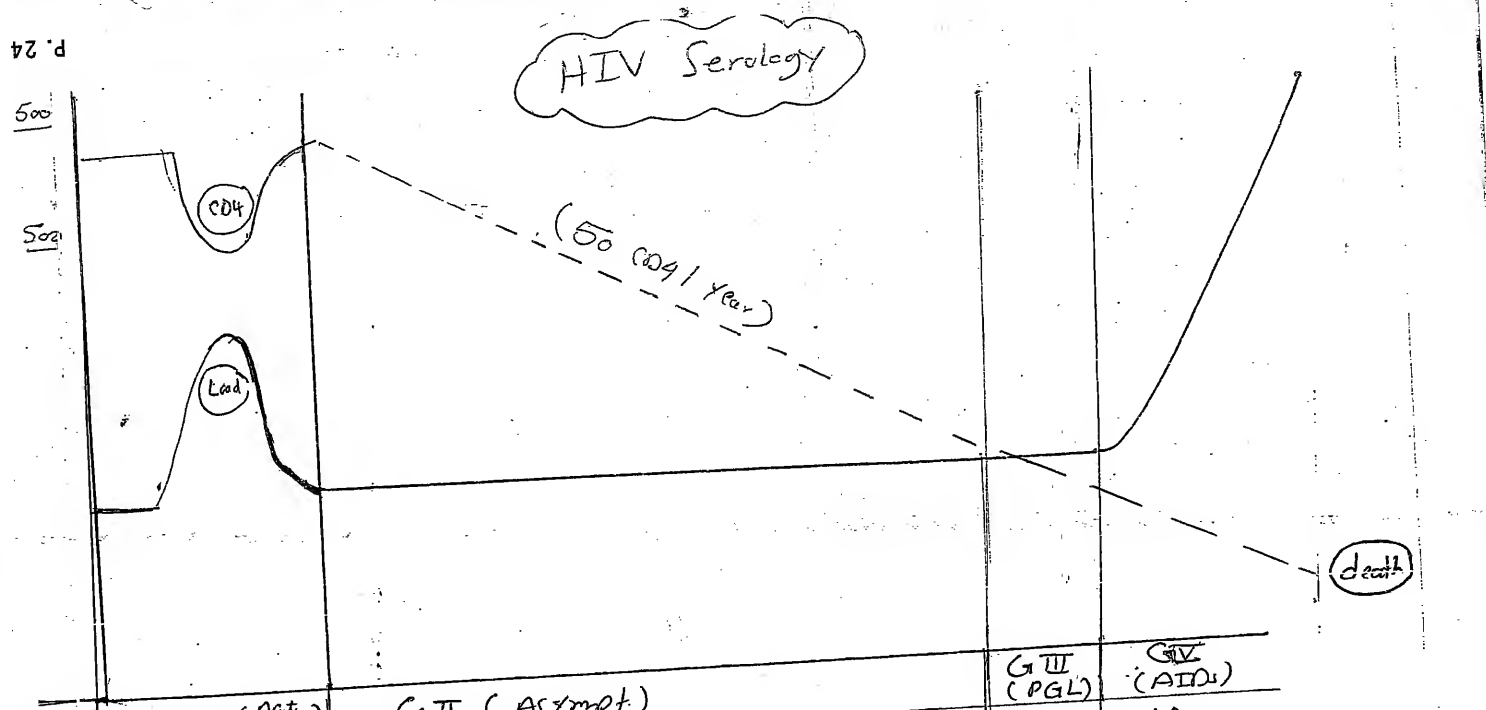
. Lymphocytes : 15 – 45 % de TWBCs (= 1000 – 4800)

↓

. CD4 → 30 – 60 % (500 – 1500)
. CD8 → 20 – 40 %
. B cells → 5 – 20 %

- NB
- leucocytic count
- CD4, CD8 lymphocyte
- plt
- S
- HBV

HIV Serology



	GI (Acute illness)	GII (Asympt.)	GIII (PGL)	GIV (AIDs)
Load	Peak ↑↑ (Transient)	• Steady (Viral set point)	• Set Point	• ↑↑
CD4	Rapid ↓↓ (11 / 700)	• Steady ↓↓ (50 cells / Y)	• Steady ↓↓	• ↓↓ (<200)
P24	+ ve	• − ve	• +ve	
gp41	− ve	• +ve	−ve	
	− ve Window phase.	• +ve	+ve	+ve

HIV

- Markers of dis. progression:

1. Lab:
   - High viral load
   - low CD4 count
   - appearance of P24 & disappearance of P24 Abs.

2. Clinical:
   - Fever
   - diarrhea
   - wt loss
   - oral Candidiasis
   - oral HL.
   - H- Zoster.

- Patients who need close monitoring:
   - CD4 < 350
   - Rapid ↓ CD4
   - ↑ viral load
   - Severe Symptoms → Candidate for HAART.

HIV in children
(Age < 13 Ys)

- **Route of Inf (MTCT)**
  - Transplacental (in utero)
  - Intrapartum (by cervical & vaginal secretion) → commonest 85%
  - Breast Feeding (±)

- **Incid**: 30% of Infants born to HIV Infected mother will be infected either Transplacentally or commonly Intrapartum.

- **Diagnosis:**
  1. HIV Ab (IgG) → [illegible]
  2. P24 Ag → may be obscured by maternal Antibodies.
  3. Viral Culture or Nucleic acid detection by PCR

- **Follow up**
  - 36-48 hrs after delivery (not Cord Blood)

Then · 3-4 Ws

Then · 3 ms Interval (by) Assessment of:
- P24
- Abs
- Viral load.

CDC 1994 Revised Criteria

For children < 13 Y.

- Category N: → No Symptoms

Category A: → mild symptoms.

- L.N
- HSM
- Dermatitis
- Paratitis
- URTI (Recurrent)

- Category B: → moderately Sympt.

- Fever
- diarrhea > 1 m.
- Pancytopenia
- Bacterial → pneumonia
- Viral → Herpes Stomatitis & Varicella
- Candidal → Oropharyngeal
- Cardiomyopathy & Hepatitis

LIP
↑
Lymphocytic Interstitial pneumonia.

- Category C: → Severe Symptoms.

↓

AIDs Criteria

(LIP) باستثناء

Clinical differences bet Childhood & Adult HIV

- more rapid progression
- Higher viral load
- Higher absolute CD4 Count
- Common < Growth Faltering (↓ Height & W.t)
  LIP (Lymphocytic Interstitial Pneum.)
- un-Common Mg
- Opportunistic Inf. → encountered for the 1st time (1ry illness may be > severe than opportunistic Inf in Adults).
- More Rapid clearance → HAART needed. → So they require Higher doses than adult Equivalent doses.

* Management:

- Triple HAART
- Antibiotics
- good Nutrition
- IVIG
- LIP → Cs
- Prophylaxis → P. Carinii & Fungal Inf.

Treatment of HIV disease

1. Prevention strategies
2. Vaccines
3. Antivirals
4. Immunostimulants
5. opportunistic Inf. ##.

---

1 Prevention Strategies:

A. Health Education
- Knowledge of Transmission routes.
- Risk reduction strategies eg Condom
- Sexual health education in schools.

B. Sex → "safe Sex"
- avoid sex (only sure prevention)
- Avoid sex & many Partners
- Condom use.

C. Blood & Blood products Transmission:
- Avoid High Risk donation.
- Screen Blood For HIV.
- Heat ## For Individual Blood products.

D. IVDAs: Avoid < Injection. / Sharing the injecting equipments.

E. Vertical transmission:
- Contraception → for seropositive women.

Pregnancy: doesn't weaken the maternal pregnancy

termination : ... — city

- Antepartum → start it as early as possible (14 ws)
- Intrapartum
  - vaginal delivery (تجنب)
  - Body Isolation of fetus.
  - Washing throughly
- Post partum: avoid < lactation / IUCD (# inf.).

Mother loading dose + شعوبي + ## of

Fetus: Early ## from birth ≤ 6 Ws.

② Vaccines: A. difficult to develop why. ??

- unknown Immune response that protect From it.
- May enhance Inf.
- greater diversity in viral genome.
- Trials Needs much < Time / Cost / Pt.

B. Vaccines under trial:

1. Subunit Vaccines.
2. live recombinant Micro-organisms
3. passive Immunization For short period.

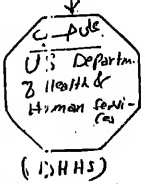
③ Antiviral treatment (HAART)

Highly active Antiretroviral therapy.

Principles:

1. Monitor < CD4 / Viral load
2. Early ## before Immunodef. become apparent
3. ↓ Viral load as much as possible (for) as long as possible.
4. use combination (مع بعض)

Indications for Duration of HAART:



1. Any pt with
   - AIDs defining illness or
   - Severe symptoms of HIV inf.

regardless CD4 count.

2. Any patient with
   - CD4 < 200 /Cmm
   - Viral load > 100.000 Copies/ml

Regardless Symptomatic or Asymptomatic.

3. Prevention of Vertical transmission:
   - Pregnancy
     - قبل الحمل: العلاج بدرجات
     - أثناء الولادة [loading dose AZT]
   - بعد الولادة لمدة أسبوع: [AZT IV]

4. Post Exposure Prophylaxis (وقائي)
   - Lamivudine (300 mg)
   - Zidovudine (600 mg) +
   - Indinavir (800 mg) +
   - (LZI)
   - (3 Combinations)

Indications to change:

1. Failed drug
   - Fever, wasting, opportunistic Inf.
   - ↑ 3 Fold viral load.
   - ↓ CD4.

   (Clinical, Viral load, CD4)
2. Drug → Toxicity & Interaction.
3. Monotherapy ⟶ Multitherapy.

Indication For Combinations:

1. Resistant
2. Improved survival
3. ↑ Efficacy.

2. Inhibitors
- Reverse Transcriptase Enz.
- protease Enz.

Reverse Transcriptase Inhibitors (RTI)

Nucleoside RTI (NRTI)

① Zidovudine = Azidothymidine (AZT)
- 600 mg 1d (tab / syr. / Inj.)
- S.E: BM–, Myopathy

(DDI) ② Didanosine:
- 500 mg 1d
- S.E: PN, Pancreatitis

(DDC) ③ Zalcitabine:
- 1-5 mg/kg/d
- S.E: PN, pancreatitis, GIT ulceral^

Nonnucleoside RTI (NNRTI)

① Nevirapine
- S.E: deposit in liver

② Delavirdine
- S.E: Skin (Rash & SJS), liver

Protease Inhibitors

SIR / VIR ③
- Saquinavir (600 mg x 3 d)
- Indinavir (800 x 3 d)
- Ritonavir (600 x 2 d)

S.E:
- Saquina → No S.E
- Indina → Renal stones & ↑ Bilirubin
- Ritona → N. GIT, Liver, DE.

- NRS
- NRTI: Faulty Blocks or Pieces when incorporated to DNA → chain terminal^
- NNRTI: -- RT enzyme.

NB . Both Reverse Transcriptase Inhibitors < Nucleoside / Non Nucleoside

inhibit RT Enzyme but by different mechanism.

→ This allow: ① ↑ efficacy ✓
② ↓ resistance ✓
③ ↓ Toxicity ✓

Triple Therapy : usually used:

قاعدة
لازم ٣ أدوية

. 2 NRTIs + 1 PI
or . 2 NRTIs + 1 NNRTI.

Other Antivirals (see steps of Viral Replication).

① Entry Inhibitors:

(Spirochetes) ← . Binding inhibitors → Maraviroc (CCR Blocker)
(Staph penetrate) ← . Fusion " → Enfuvirtide
. Uncoating " → Etravirine.

② Integrase Inhibitors : Elvitegravir.

③ Transcription & Translation Inhibitors:

. Tat inhibitors
. Antisense Constructs
. Ribavirin

④ Viral budding Inhibitors:

. Interferon ✓
. Antibodies
. Ligands.

⑤ Natural inhibitors:

Cavities depot of Capsid P24 protein of viral replicat & assembly ← Cyclosporin A (Vivecon).

⑥ Broad Spectrum inhibitors

Mushroom Extracts

USA HHS

لو فاحص حامل وعندها HIV
طريقة الولادة ؟؟

C.S Preferred if.

- didn't Receive Prenatal Care
- " " ANY HAART
- Viral load > 1000 Copies/mp.

Vaginal preferred if.

- Received Prenatal care
- Viral load < 1000 Copies/ml

حتى كلا الكائنين تقل اذيتن

① IV AZT : 3 hrs before labor
② IV AZT : during labor
③ ↓ Fetal Exposure to mothers blood & avoid < Forceps Vacuum.
④ IV AZT for Fetus From birth to 6 wks.

Human Herpes Virus group.

As in dermat.

Cap I

. Herpes: Greek word. means "To Creep or Crawl" in Reference to the Spreading Nature of the dis.

. Herpetiform: lesion that is similar to HSV (multiple Grouped vesicles on erythematous base or similar to Herpetic ulcer). Clinical, superficial Erosion.

. Human Herpes Virus group characters:

① . double Stranded DNA
② . Replicate intranuclear.
③ . produce: 1ry infect → Latency → Reactivat. & Recurr. inf.
- 1ry infect: at site of inoculat
- Latency: in Nervous or Lymphoid Tissues.
- Reactivat. & Recurr. inf.: in Later life. either Spont. or by ppt. agents.

Classification of Human herpes viruses "HHVs"

HHV 1	Skin & oral mucosa → H. labialis.
HHV2	Genital areas → genital herpes.
HHV, 3	Varicella zaster.
HHV, 4	Epstein-Barr virus.
HHV, 5	Cytomegalovirus
HHV, 6	Exanthem subitum (roseola infantum).
HHV, 7	Associated with roseola.
HHV, 8.	Associated with KS. / Lymphoma. "oncogenic virus"

Last 2 Ass

	HHV	Site of latency	Manifestations	
α-HV	HHV1 (HSV1)	Nervous syst. "Neurons"	H. labialis	1° & recurrent
	HHV2 (HSV2)		Genital herpes	
	HHV3 (VZV)		Chicken pox	1°
			H. zoster	2°
β-HV	HHV5 (CMV)	Immune syst. "Lymphoid tissue"	Asympt. mono-like	
	HHV6		Roseola infantum ✓	
	HHV7		Associated with Roseola ✓	
γ-HV	HHV4 (EBV)		Infectious mononucleosis.	
	HHV8		KS associated herpes virus	

Herpes.

Herpes Simplex Viruses

(HSV1 & HSV2)

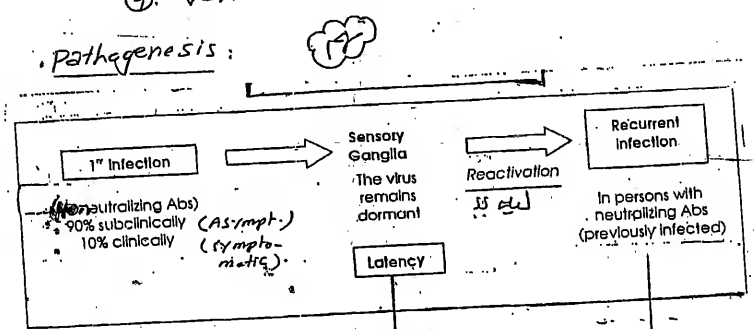
- Non genital H-SV usually affect Non genital skin & MM → Herpes labialis (Above Waist inf.)
- Genital HSV usually affect Genital skin & MM → Herpes Genitalis (Below Waist inf.) the Genitalia (10-40%)

NB Nowdays HSV1 may affect oral & MM & HSV2 may affect non Genital skin (d.t Common practice of oral sex).

. Mode of Transmission:

1. droplet inf. (in HSV1 labialis)
2. Contact with active lesions (Vesicular lesions before Crusting) / infected secretions.
3. Sexually Transmitted (HSV1 & HSV2)
4. Vertical Transmission (From mother → Fetus)

. Pathogenesis:



Site of latency

- HSV1 → Trigeminal Ganglion
- HSV2 → Lumbo-Sacral Ganglion (Thigh, buttocks, genitalia, L-L)

. It may reinfect:
- face
- Oropharyngeal MM
- Ocular MM

Comment on:

- incid. of recurrence
- No of recurrences
- CIP of N

Types of Inf. Caused BY HSV

- **Initial or First Episode Inf.**
  - **1ry (True 1ry inf.)** → Never infected by HSV1 Nor HSV2
  - **Initial Non 1ry inf.** → individual previously infected by one Type & develops inf. by the other Type.
- **Recurrent Inf.** (Clinically 3 Types)
  1. Symptomatic (<50%)
  2. Symptomatic unrecognized (>50%)
  3. Asymptomatic

Clinically: 10% Sympt. & 90% Asymptomatic

- Recurrent infect
  - Causes of reactivat
  - Incid
  - No of Recurrences/Y
  - Clp.

- Causes of Recurrence: either
  1. Spontaneous
  2. or predisp. factors
     - Stress
     - Sex
     - Menses
     - Fatigue
     - Fever
     - UVB (HSV1)
     - Immune-Suppression

Symptoms of recurrent HSV are similar to those of primary HSV infection

Recurrence	HSV1	HSV2
• Causes • Incid.	• ≃ 50%	• ≃ 90%
• No of Episodes	• ≃ 1 / year	• ≃ 6 / year

So HSV2 recurs more Common & more Frequent > HSV1

• Types of recurrent inf.

1. Symptomatic: classical lesions & Symptoms of HSV.
2. Asymptomatic: the virus descends from the dorsal roots along the nerve & replicate at skin surface or MM & out producing lesions or Symptoms (no S. nerves) (subclinical)
3. Symptomatic Unrecognized: المريض بيجيله أعراض شبيهة أعراض الـ HSV بس مش بيعرف إنها HSV لأنه مش بيروح للدكتور (non classical S & S of HSV inf.)

↓

• So that Periods of Transmission or shedding of the virus may occur during:

1. Symptomatic shedding: shedding during active symptomatic lesions. ← Less common Period of Transmission.
2. Asymptomatic shedding: shedding during absence of Clinical lesions. (the virus descend along the nerve → replicate & out producing lesions).
3. Unrecognized Shedding: المريض ماعرفش إنه عنده HSV عشان مش شكل إصابة كلاسيكية

← The Main & The Most important Periods of Transmission.

Diseases Caused by HSV:

1. 2 main diseases: Oropabial H.S (H. labialis or facialis) / Genital H.S (H. genitalis or progenitalis)
2. Other Herpetic inf:
   - ocular H.S
   - *. Neonatal H.S
   - Herpetic whitlow
   - Herpetic Sycosis
   - H. Gliadialorum
   - *. Eczema Herpeticum
   - *. H. Encephalitis
   - *. Herpes in Special Situations → HIV / Immuno-Compromised.

Orolabial H.S (Commonest HSV1 inf.)

⊙ Viral Transmission
- HSV1++
- HSV2 ±

IP: 3-7 dr.

Primary infection → (Herpetic Gingivo-stomatitis) (MN)

10% Symptomatic

90% Asymptomatic

a. Prodromal (marked) < Systemic: FAHM, L.N (tender)
Local: discomfort, burning, Tingling, Numbness & Tenderness.

b. Eruption (lesion): ⊙ presentation acc. to age:
- Vesicles → NB: Grouping
- Site
- Healing

[Gingivostomatitis: in children.
Pharyngitis: in young adults.] → 3 sites: oral mucosa, pharynx, gingivae.

⊙ more numerous, Less grouped vesicles on erythem.

base → Rupture → crusted. 2-3 wks → Resolut°

Healing ~~> 2-3 wks.

↓

Latency (in Trigeminal Ganglion)

↓

Predisposing Factors For Recurrence
Specially UVB (sun.)

↓

Reactivation

↓

Recurrent episode. → (Cold Sore, Fever blister)

NB at Site
Vesicle
- dome shaped
- umbilicated.

a) prodromal ↓ as in 1ry inf. but less marked
Neutralising Ab ↑ ~ 1

b) Eruption (lesion): - fewer No of Vesicles + Marked grouping.
- Healing ↓ in 1-2 wk.

6

- Site of lesions:
  - Commonest lip (Vermilion border)
  - less Common
    - perioral
    - perinasal
    - cheek
    - ear lobule

No MM affect

d) Recurrence: ≃ 1/year.

Note the difference bet. 1ry inf. & Recurrent inf.

- Prodroma
- lesions
  - No. of vesicles
  - grouping
  - Site
  - Healing

- Note that
  - 1ry orolabial H.S : Called Herpetic Gingivo-stomatitis
  - Recurrent " " " : Called Cold Sore = Fever blister

- what is the Commonest predisposing Agents?: Sun (UVR).

1ry infection	Recurrent Infection.
Ip: 3 - 7 days	. Reactivation either Spont. or under effect of Certain Agents.
. usually: Children (1-5 yrs) or young adults.	. Adults.
. usually: Asymptomatic & if Symptomatic it will be more severe.	. Symptomatic & less severe.
. Prodroma: Marked	. Less marked
. Eruption: (lesion)	
Ⓐ. more Numerous Vesicles & lesser grouping.	: Fewer vesicles & more grouping.
Ⓑ. MM: usually affected	. usually (not) affect the MM.
Ⓒ. Healing: 2-3 wks	lesion affect the same Region but not the exact area. Healing 1-2 wks

Genital Herpes
(Herpes progenitalis)

- **Def.** infection of Genitalia by HSV.
- **AET & Transmission:**
  - HSV_2 (70%) → Sexual intercourse.
  - HSV_1 (30%) → oral sex.
- **Types of infection:**
  1. True primary inf.
  2. Initial Non primary inf.
  3. Recurrent inf.
- **Periods of Transmission:** ± during
  1. symptomatic inf.
  2. Asympt. shedding
  3. Sympt. unrecognized.

Most ↑ assoc. → 2 & 3

CIP

(A) primary inf. (< 90% Asympt. / 10% Sympt)

1. IP: 2 ds – 2 ws (usually 3–7 ds)
2. Prodroma < local / systemic
3. lesion (No ↓ grouping of vesicles).

Site

- Rectum
  - ♂ ↓ Homosex.
  - ♀ ??
- ♂
  - painful Ensive balanitis
  - commences at glans, shaft & rectum (in Homosex.).
  - ← Vesicular ulcerated lesions.
- ♀ (Birth).
  - Vulvitis
  - Vaginitis
  - ✓ Cervicitis (Most Common 80–90%)
  - Buttock / perineal

Healing: ↓ 2 – 3 Ws.

B. Recurrent inf. (Reactivat.):

1. Recurrent: cause, incid, No., Types
2. Prodroma — Local(+) (Mild) / Syst.(-)
3. lesions Col. & grouping of vesicles

Site: → same Region but not the exact area (generally below Waist).

Healing: 1-2 ws.

(H. labialis اقل)

NB [1] Recurrent inf. usually (>50%) ASympt. or Sympt. unrecognized.

[2] Initial Non 1ry inf. is more mild > True primary inf. (إلا) Neutralising Ab. "Cross Reactivity"

Complications of H. Genitalis:

- More Common in:
  (1.) Women (2.) 1ry inf.

HAEM

- include:
  1. 2ry bact. inf. (Most Common) ± Scarring
  2. Extragenital lesions (20%, Cut. or Syst.)
  3. Urine Retention (15%): d.t.
     - Lumbosacral radiculopathy
     - Reflex pain inhibition d.t. intraurethral lesions.
  4. ASeptic Meningitis. (Fever, Headache, Vomiting & Photophobia).
  5. Neonatal H.S.
  6. Cancer Cervix.
  7. depression / Psychosexual problems.
  8. HAEM
  9. ECZema Herpeta

So Recurrent HS of Cervix → do cytological Smear/Y.

Neonatal H.S

- Mode of Transmission:
  1. Antepartum (Transplacental): (5%)
  2. Intrapartum: during delivery (85%)
  3. postpartum: non maternal source (kissing by infected adult) (10-15%)

  (So there are 2 sources: Maternal & non-Maternal).

- Risk of inf.
  - A. Episode: 1st Episode attack of mother is more dangerous > recurrent Episodes in causing Neonatal inf. Why?? (in recurrent Episodes the fetus is protected by Maternal IgG)

    inCid acc. to the episode.

    ① True 1ry Episode → 50%

    (non 1ry 1st episode) → ② initial non 1ry → 30%

    ③ Recurrent episodes & asympt. shedding → 0-4%

  - B. HSV1 > HSV2 (despite its less common).
  - C. presence of active lesions at time of delivery.
  - D. PROM
  - E. using fetal scalp Electrode.

- NB: • The most serious is women é 1ry inf. & having active lesion caused by HSV1 at time of delivery. However most cases are d.t. Asympt. shedding.

CIP

Antepartum (Transplacental)

- Abortion
- IUFD
- Prematurity
- Cong. Anomalies:
  - Microcephaly
  - Microphthalmia
  - limb hypoplasia
  - Encephalitis
- Skin affect: extensive cong vesicles & Erosions → Healing ē reticulate scarring & usually Fetal

Intrapartum (Commonest)

3 Types of affect:

1. SEM: localized inf of skin, Eye & mouth.
2. Localized CNS affect.
3. Disseminated inf. (Multiple organs) (CNS, Lung, Renal).
4. Non specific Symptoms as: irritability, poor feeding & lethargy.

Complications

- Seizures
- Psychomotor retardat
- Spasticity
- Blindness
- Learning disabilities
- Death.

NB:
- Transplacental Transmission: has poor prognosis ē High Morbidity & Mortality
- Intrapartum Transmission: has better prognosis ē > 90% develops normally.

Eczema Herpeticum

(Kaposi Varicelliform Eruption)

HSV inf (1 or 2) + any of the following condition :

- AD
- SD
- Scabies
- Ichthyosis
- Darrier
- Hailey-Hailey
- Pemphigus
- Pemphigoid

(usually First Episode)

Spread of HSV throughout the diseased areas (Eczematous Areas)

(dt: C.M.I of Impaired host immunity)

C/P (DNNZ):

1. If : 5-12 ds after exposure to Individual ē 1ry episode of HSV inf. (either symptomatic or Asymptomatic)
2. FAHM
3. Clusters of itchy & later painful blisters start usually at head & neck on active or healed site of previous skin dis (e.g. AD) → 7-10 ds → New patches appears at others diseased areas which may become Generalized → 2-6 wks → ± Healing ē small white scars.

(Si - Severe e.c.zema)

Fever & Severe pain vesicles Punched out Erosions → Clue for Diagnosis

. the lesion clinically : monomorphic, umbilicated Vesicles filled ē clear, cloudy or Hgic fluid → Hgic Crust formation → painful punched out bleeding Erosions.

4. 2ry bact. inf. may occur
5. In Severe Cases → systemic organ affection e.g. Eyes, CNS, Lung, Liver → fatal

N.B: other viruses may cause Eczema Herpeticum

- Small Pox → Vaccinia virus → Eczema vaccinatum
- Hand-foot & mouth dis → Coxsackei v A16 → v Coxsackium

NB when caused by HSV it is called Ecz. Herpeticum but when the causative virus is unknown it is called:

~ Kaposi Varicelliform Eruption

Treatment: (1.) ACV or VCV : oral or IV

(2.) Antibiotic

(3.) Consult ophthalmologist if Eye affected

Ocular H.S (Herpetic Keratoconjunctivitis)

- Keratitis, conjunctivitis, Corneal ulcer & ± Erelid affect.
- preauricular L.N
- 2nd commonest Cause of Corneal blindness in USA
- if HSV1 or HSV2:
  - if neonatal → usually HSV2
  - if older than Neonate → HSV1

Specific Trifluridin (Virostatic) (antiviral)

Herpetic whitlow ??

digital H.S infection occur in:

- Children : oral H.S → HSV1
- dentists & medical personnel → HSV1
- digital/genital Contact → HSV2

Herpes Gladiatorum (rugby)

H.S infection occurs among wrestlers or during practice & sports at close contact.

Herpetic sycosis : H.S inf. of beard & moustach of Adult → Viral Folliculitis

Herpes infection in special situations

[A] In immunocompromised: (AIDS, HIV)

1. Chr. ulcerative H.S : persistent erosions & ulcers (in Face & Perianal area) (ulcers Superficial confluence)
2. Acute Generalized : (Varicella like) : wide spread Vesicular eruption (as Varicella) → death
3. disseminated Visceral
4. More Frequent shedding
5. ACV Resistant H.S (IV use) < Foscarnet / Cidofavir

- Verrucous
- Exophytic
- Pustular
- ulcerative

lesion ±

[B] HSV + HIV : → more Severe outbreaks, More Frequent Viral shedding

use Anti HIV + ACV (if No Resistance).

Q. How to differentiate bet. 1ry & Recurrent attacks. (Sec ano - labial Hs)

Q. Whole duration of dis outbreaks??
- Primary attack : 3 ws.
- Recurrent " : 1 w.

Q. does Frequency of Recurrence will ↓ over the time (without H)??
- over longer periods (3-5 Ys) Frequency of outbreaks will ↓.

Q: why genital Herpes is a problematic disease??

Friend of life + . because it is not curable so → associated ē

social stigmata:
- Emotional stress
- Anger
- depression
- Guilt

→ So psychological aspect should be evaluated well.

. Diagnosis of H.S

(1) Tzanck smear: bed side test
- Rapid preliminary procedure that can be used in office.
- Nonspecific (Can't diff. bet. HSV1 & HSV2 or even VZV)
- Results → 60-90% accurate
  → 3-13% False ve.
- Method: Recently developed vesicle (48 hrs) → dressed → Absorbant Gauze for Fluid → swabbing the base then examined by Mic or stained then examined → Multinucleated giant cells. (Tzanck)

(Hel serum obtained # Bleeding)

(2) DFA ← Rapid, sensitive, diff. bet HSV1 & HSV2 [الصورة لاكثر استخدام في تشخيص المرض]

(3) Cul ture: differentiate bet. different types & Can be available within 2-5 days. (on Hela Cells)

(4) PCR: used as Cul ture; used to detect DNA of the virus in CSF

(5) Serology:
- 1. detect asympt. carriers.
- 2. determine inf. Rate in various Popul.
- 3. detect couples at RISK for Neonatal H.S

2nd generation ELIZA

Western Blot: Very good for detect & Glycoproteins: gG1 → HSV1 & gG2 → HSV2

WBIS FDA For det & prev. ens.

5. Histopathology:

① Ballooning degen of KCs with intra-nuclear Inclusion Bodies (degeneration & Margination of chromatin) → Blistering (at level of St. Spinosum)

② Multinucleated giant Epid. Cells:
Formed by fusion of infected KCs
nuclei are fit or molded together as pieces of puzzle (Clark)

NB: Dx depends on lesional Morphology!
- Acute Vesicular lesion → Tzanck.
- Crusted, eroded or ulcerative lesion → culture

Complications of HSV & its types:
① 2ry bact. Inf.
② Corneal ulcer, opacity
③ dissemination → Hepatitis, encephalitis & Pneumonia.

④ Pt →
4. HAEM (Herpes ass. Erythema Multiform):
- H.S is the commonest cause of Recurrent EM
- usually after ⑨ days.
5. Neonatal H.S
6. Eczema Herpeticum
7. Cancer Cervix.
8. Complications of genital

Treatment of HSV inf

- Prophylactic
- Curative (active)

A. For Herpes labialis (HSV1):

1. Avoid triggers e.g UVB → give sunscreen.
2. prophylactic Antivirals (before)
   - 2 4 hrs before or at morning of the procedure & For 2 ws after that (FCV: 250 x 2 / VCV: 500 x 2)

B. For Herpes Genitalis (HSV2):

1. Avoid sex: (the only sure protective method).
2. Condom use: prevent transmission from ♂ to ♀
3. Vaccine: Glycoprotein D HSV2 Vaccine (under trial)
   - for prevention of HSV2 in Women That's Sero-ve for HSV1 & HSV2
   - [Also: lupidone G & H Vaccines]

C. For prevention of Neonatal HSV:

1. Cesarean sect: for all cases ē active lesions or prodromal symptoms or ē pH ē HSV inf.
   - disadv: doesn't prevent inf. / Expensive. / ↑ Morbidity.
2. Recently: Measures taken if: the ♀ & ♀ are sero-ve / the ♀ sero-ve & ♀ sero-ve / ♀ ē Hx of recurrent HSV1

Measures For:

- Wife:
  - Avoid Sex in last trimester
  - Vaccine (see above)
  - ACV: Suppressive Ht in Last Trimester (at 36 WD) ↓ incidence of Vaginal & Transplacental
- Husband:
  - Condom
  - ACV: Suppressive Ht. (during last trimester)

(Sero-ve ... Sero-ve)

D. Prophylactic Chr. Suppressive antiviral therapy

For recurrent inf. (HSV1 & HSV2):

- Indications:
  1. recurrent inf. > 6 outbreaks/Y.
  2. recurrent HAEM > 4 - 1 Y.
  3. physically or emotionally severe outbreaks.
  4. Insufficient prodrome to benifit from Episodic Ht.
  5. Immuno Suppression (post transplant)
  6. Suppressive Ht for Sero-Ve Couples.
  7. post herpetic vitiligo.
- Dose, → see Ht of H. Genitalis.
- NB: → Resiquimod 0.01% gel is used
  - Topically applied Immune response Modifier used to ↓↓ recurrence.

Active (episodic/curative) treatment of HSV infection

- Topical
- Systemic
  - ACV
  - VCV
  - FCV

الجدول

① ACV 5% Cream: دهان كل ٤ ساعات لمدة أسبوع — على كل HS ٤

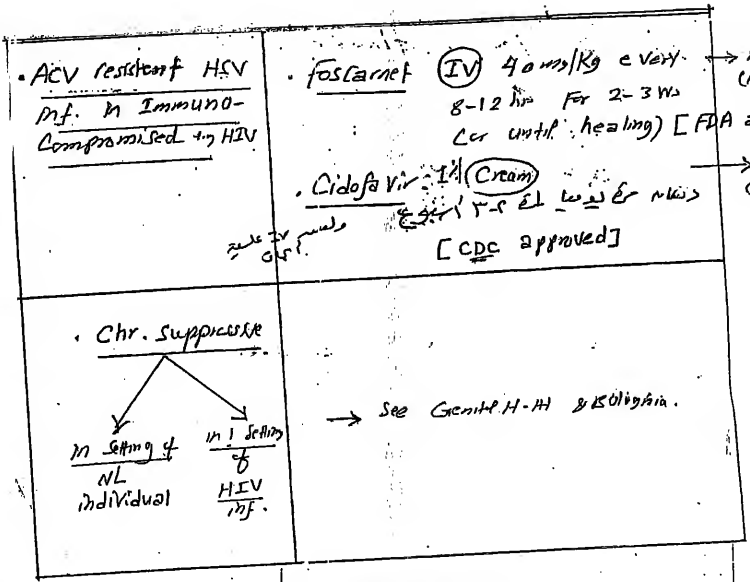
② Penciclovir 1% Cream: دهان كل ساعتين أثناء اليوم (ما عدا الليل) لمدة ٤ أيام

③ Docosanol 10% Cream: دهان ٥ مرات في اليوم لمدة ١٠ أيام كحد أقصى

→ FDA approved for Herpes Labialis

④ ACV + Topical Cs < Hydrocortisone 1% / or / fluocinonide 0.05%

Type of Inf.	Treatment.
"Recurrent" H. labialis إعتراض هيباتا دماغي (encephalitis)	• ACV: (400) → ٥ مرات يومياً لمدة ٥ أيام. (Not FDA approved.) • VCV: ٢ جرام مرتين يومياً لمدة يوم. → لمرة واحدة • FCV: ١٫٥ جرام جرعة واحدة. → لمرة واحدة
✓ • H. Genitalis	< 1st attack / Recurrent.
✓ • Neonatal HSV inf.	• ACV: (IV) 10mg/kg every 8 hrs for 10 - 21 d
✓ • Immunocompromised	• ACV < oral: 400 X5 /d / or / IV: 5mg/kg/8hr • VCV, • FCV } أقراص مرتين يومياً Durat° until all lesions healed.



• General Considerations:

A. Guidelines For Antivirals in H of HSV

① should be given during the 1st 48hrs | or during the prodromal (tingling, Numbness, Burning) to be effective.

② Its value is: ↓ pain, ↓ shedding, ↓ Healing time.

③ Chr. suppressive H value is:
- ↓ Asymptomatic Shedding by ≃ 95%
- ↓ recurrence by ≃ 80-90%.

B. Topical ACV Cream: FDA approved For limited Mucocut Inf. in Immuno Compromised while its use in Immuno Competent (may) be not effective & may cause resistence to systemic ACV

C. Penciclovir 1% & Docosanol: → FDA approved For recurrent H. labialis

D. Systemic ACV: not FDA approved For H. labialis but used by authors / FCV/VCV → approved.

Treatment of Herpes Genitalis

A. 1ry attack → 10 days (7-10).

- ACV (3) قرص ٣٠٠ يوميا | or 200 mg x5
- VCV (4) قرص ٤ مرات يوميا
- FCV (3) قرص ٣ مرات يوميا

1 tab:
ACV 400 mg ✓
VCV: 500 ✓
FCV: 250 ✓

B. Recurrent attack: For 5 ds (5-7 ds).

- ACV → 3 (ad.ry)
- VCV → 2 tab/d
- FCV → 1 tab/d

C. Chr. Suppressive Therapy (≥ 6 Recurrences/Year)

- ACV
- VCV
- FCV

} start ē 2 tab/d For (1 year) & Reassess (for) frequency & severity.

لو مريض له < 10/y: أعطه يوميا
لو مريض له ≥ 10/y: أعطه يوميا

يقلل shedding بنسبة ٩٠٪
يقلل recurrence بنسبة ٨٠٪

تأمل
- For life
- or Stop after 10 ys or ACV (6 ys) & VCV/FCV (1 y)

Warts (Verrucae)

(1)

Def. Benign epid. proliferations (Tms) caused by Human papilloma virus (HPV) Inf. of < Skin & MM

HPV belongs to Papovirus group w are:

- slowly growing
- double stranded &
- Naked. (no envelope: so resist drying (freezing) & lamb)
- > 100 types of HPVs discovered.

Mode of Transmission:

1. Contact / Direct e.g. المباشر
   \ indirect e.g. الغير مباشر
   autoinoculation. (causes → local spread.)
   e.g. أصابع القدم "Pseudo koebner"
2. Sexually transmitted.
3. Vertical: perinatal during vaginal delivery. Laryngeal papillomatosis

Types of infection:

1. Clinical: Lesions seen by Gross inspection.
2. Subclinical: lesions seen only by aided exam. (acetic acid soaking). مجهر
3. Latent: - presence of HPV virus or viral genome in apparently N.L. Skin.
   - Thought to be common specially in Genital warts & explain in part the failure of destructive methods to eradicat warts.

Why Recurrence is common → Ø.E.

HPV Classification

- According to Risk of Transformation
  - Non Risky group → 4 types: 1, 2, 3, 4
  - Low Risk group → 6 & 11 types
  - High Risk
    - usually: 16, 18, 31, 33, 45
    - Also:
      - HPV6 (±)
      - HPV58
- According to Type of infection → (See below)

أنواع كوبس جدًا

- 6 & 11: Low risk
- 16 & 18, 31, 33, 45: High Risk

HPV infection: "Ag"

Genital

High Risk HPV (16, 18)

- Bowen's dis
- Bowenoid papulosis
- High grade intraepithelial Neoplasia.
- Giant Condylomata Accuminata of Buschke-Lowenstein → استثناء إنها سببها (HPV6)

Low Risk HPV (6, 11)

- Condylomata Acuminata
- Low grade intraepithelial Neoplasia. (CIN)

Non genital

Cutaneous

- Cut. warts.
- EDV

Mucosal

1. Laryngeal: Papillomatosis < Cancer
2. Conjunctival
3. oral
   - Papillomatosis
   - Cancer
   - Leukoplakia
   - Heck's dis.

DD لترسوال

+ Cowden's dis Syn.

- Cancer (Thyroid, Breast, trichilemmoma, oral papilla)

(cobble stone)

NB
- كلنضع سه لهيزوس سيفتش نقاط معينة للعدوى.
- سكس لنوع لواحد يحل عدوى غاى كنة مختلفة.

سؤال لمتزن: Common ⇌ Genital

(8)

HPV ... Genitalia ...
Classified into

- Low Risk or Benign types.
  - ≃12 types of HPV
  - Commonest: 6 & 11
  - ① Condylomata Acuminata. (Pl. Condyloma Accuminatum)
  - ② Low grade IN
- High Risk or oncogenic types
  - ≃ 15 types of HPV.
  - Commonest: 16 & 18 (also 31, 33)
  - ① Bowenoid papulosis
  - ② Bowen's dis.
  - ③ Buschke-Lowenstein Tm. (استثناء سببه HPV 6)
  - ④ Intra epithelial Neoplasia (High grade)
    - Vulvar IN (VIN)
    - Cervical IN (CIN)

Condylomata Acuminata (Genital Wart).

- Most common STD among sexually active young adults in USA & Europe.
- Most infections are Latent or subclinical & this is Responsible for high Incidence & Recurrence following Rx.
- Genital HPV inf. of great importance in women than men (♀) d.t Risk of cancer cervix.
- Genital HPV inf. closely linked to Cancer: Cervix, glans, anus, Vulvovaginal area, Perungual area.

Natural Hx of Genital warts:

- Most cases → lasting (1-2 y) then resolve.
- few cases → persist.
- fewer " → Cancer.

Other factors that ↑↑ Risk of Malignancy of HPV:

follow up & pap smear.

1. Location of infection → Transition Zone eg Cervix, Anus
2. Smoking
3. uncircumcision (in ♂)
4. Immunosuppression → Highest Risk
5. Sex: early: before 17 y use; Multiple: 6 or more; & Prostitutes.

HPV Types: 30 types may be responsible for Genital Warts & more than one type usually exist in one patient.

Type: HPV: 6 & 11 be. (Bg or Low risk to Transformed to Mg).

Site: may affect:

♂ → penis, scrotum, anus, intraurethral (Hematuria or Allergy stream), anus, perineum, intraurethral.

♀ → vulva, cervix

Clip: 2 clinical Varieties: according to the site:

- on dry surfaces (penis, scrotum) → Hyperkeratotic Common wart like Papules
- on Moist opposed surfaces (Perianal/Perineum) → Cauliflower mass
  - Pedunculated
  - Flesh Colored
  - Verrucous
  - Bleeds easily

Tx: Podophyllin.

Genital warts in children Transmission may occur d.t.:

1. Vertical Transmission perinatally. (اثناء الولادة)
2. digital autoinoculation
3. Fomites (الملوثة)
4. Social non sexual contact
5. Sexual Abuse. / إساءة جنسية وخصوصا للأطفال

- Transmission acc. to age:
  - (in) 1st year غالبا → Vertically
  - Age > 3 Ys: غالبا → Sexual Abuse.

- Spont. Resolution often in (75?) % Cases.

NB annual Pap. Smear should be Taken From:

1. female ī genital wart
2. Homosexual Male ē Peri-anal Wart
3. any genital wart in Immunu-Suppressed

Bowenoid Papulosis (For details see Skin Cancer)

- HPV: 16 & 18
- Site: may be < Genital: penis, vulva & perianal.
  extragenital: Face & neck
- Clinically: Flat, sessile, Hyperpigmented papules that difficult to be differentiated from condyloma Accum.
- path: Abnormal epithelial maturation & cellular atypia closely resembling Bowen's dis.
- progression to invasive SCC more in lesions of < penis, cervix, vagina, rectum.
- Females < with Bowenoid
  with their husbands have Bowenoid → Risk of cervical Dysplasia

Giant Condyloma Accuminatum of Buschke & Lowenstein

- there is a type of SCC called Verrucous Carcinoma or can occur in 4 sites: (all may be caused by HPV)
  (Ackerman Tm) → ① oral cavity → oral Florid papillomatosis
  ② Genitalia → Buschke & Lowenstein Giant Cond.
  ③ Planter aspect of foot (sole) → Epithelioma Cuniculatum.
  ④ Gottron Tm: skin
- Verrucous Carcinoma chy < well differentiated
  slowly growing
  Locally Mg (rarely metastasize).

giant verr. ← Giant Condyloma Acc. of Buschke & Lowenstein:

- Sol. keratosis
- black genital wart
- condyloma accuminata
- rare aggressive wart like growth (Fungating condyl. like)
- Caused by HPV 6 (16, 18 with Carcinoma)
- Site < Common: glans & prepuce of uncircumcised ♂
  Less: perianal & vulvar.

DD of psoriasiform les

Basicle cell Carcinoma

Bowen's

extramammary paget's

Multiple plane wart

Acrokeratosis verruciformis

Epidermodysplasia Verruciformis

Diagnosis of Genital Warts: (12)

(1) Acetowhitening:

Aim
- [a] For detection of subclinical inf. of Genitalia.
- [b] detection of early lesions under foreskin.
- [c] determine extent of infect. in patients e multiple recurrences.
- [d] define the area necessary for application of Ht

Method
- Acetic acid 5% (vinegar) applied for 5–10 mins → small macular white lesions.

False +ve: may occur e candida, Dermatitis, psoriasis. If present: Antifungal + Hydrocortisone 1% → Repeat testing after 2 wks (if +ve) → Biopsy & Histopath. exam. for HPV.

(2) Histopathology: (done before Ht of any suspicious Lesions).

Signs
- Acanthosis
- Papillomatosis
- Koilocytosis: cells of st. Malpighii appear e chic
  - Cytoplasm: vacuolated
  - Nucleus: Round & Hyperchromatic e perinuclear halo.

(3) PCR (detect Viral DNA) [latent inf.]

(4) Pap Smear: For any Immunosuppressed. e Genital W.
- Women: e Genitalws
- Men: e anal or perianal warts.

(5) Sexual Partner exam: For detect of any Subclinical inf.

NB: diagnosis of:

Subclinical inf.	Latent inf.
BY: acetowhitening	BY: • PCR • Immuno-peroxidase → detect the viral DNA inside the Nucleus

(15) D.D of Genital warts = Causes of Papular / nodular Genital lesions

DD of condyloma acuminata

Sexually transmitted diseases

3
- **Condyloma latum (syphilis):** broad-based, smooth-surfaced lesion.
- **Herpes simplex virus (HSV):** vesicular eruption with red base and ulceration.
- **Molluscum contagiosum:** umbilicated yellowish papules with central core.

Common benign skin lesions

3
- **Nevi:** typically raised, but pedunculated types may occur.
- **Ectopic sebaceous glands (Fordyce spots):** small, yellow papules on genital and oral mucosa.
- **Pearly penile papules:** circumscribed papules, 1-2 mm in diameter, usually over the proximal edge of the glans penis (considered normal anatomy).

Neoplasms *(biopsy required if suspected)*

3
- **Bowenoid papulosis:** [redacted], single or multiple rough papules, 2-4 mm in diameter, flesh-colored to red-brown, recalcitrant to usual wart therapies.
- **Malignant melanoma:** typically single, may be flat or raised with variable color and shape.
- **Giant condyloma of Buschke-Löwenstein tumor:** low grade, locally invasive malignancy that can appear as a fungating condyloma.

=flat Sessile pigmented rough

Pigmented flat sessile.

do Biopsy if there is Controversy."

Cond. Accuminata	Cond. Lata
. HPV	. T. Pallidum
. Cauliflower . Flesh colored . Verrucous Surf.	. Flat . Grayish . Smooth Surf.
. Pedunculated(50%)	. Sessile
. bleed easily	. don't Bleed esily.

. NB: . Malignant transformation in non genital wart is Rare But may occur & so called: Verrucous Carcinoma that may occur on any area but Commonest is planter Surface (epethiloma Coniculatum).

. A typical, non Resolving wart on hand / Foot / Periungual unit should be Biopsied to Rule out SCC as can mimic wart specially in the Region of Nail unit.

Treatment of Condylomata (22)

Goal of Tt: Removal of exophytic lesions & Amelioration of symptoms.

- no Tt has been shown to eradicate HPV Completely
- d.t Common Latent & subclinical infection. (So)
- it may be considered Friend of Life (as H.S.V2)

- ① - Inf. about high incid. of recurr
- ② - No relation (+) ext. Tt & recurr
- ③ - ∃ any modality continue Tt to 3 months to say failure
- ④ Benign neglection
- ⑤ No aggressive Tt
- ⑥ Friends of life

Treatment

Prophylactic

1. Avoid sex
2. Safe sex
3. Condom
4. Vaccines
   - Gardasil (HPV4) [against HPV 6, 11, 16, 18] (E) → For ♂ & ♀ at 9-26 y.
   - Cervarix (HPV2) [against HPV (6, 11)] → For ♀ at age 10-25 y.

Dosage: 1 day, 2ms / 6 ms. (3)

Efficacy: الأفضل بتطعيم للذين لم يصابوا بالعدوى وتكون حمايتهم أطول.

- ↓ Genital wart (62%)
- ↓ High Grade CIN

Curative

1. Antimitotics
   - podophyllin resin
   - podophyllotoxin
2. Anti Neoplastic
   - 5FU
   - Cidofovir
3. Desiccants → TCA
4. Immune response Modifier:
   - Imiquimod
   - IFN α2b
5. Surgical Methods
   - Electrocautery
   - CRYO
   - Endoscopic surgery
   - Co2 laser.

الكرة

∴ Podophyllin Resin 25%
in Tr. Benzoin (مذيبة إنتاجي)

Crude
. extract of dried roots of the May apple plant.
. Contain many ingredients: the most active is Podophyllotoxin
. used ← Tr. Benz / Alcohol / Collection (10-35%)

. مس كل أسبوع يطفى بعد مرور ٦ ساعات وتكرر طريقة العلاج ٦ مرات

. C-I ← Pregnant (Teratogenick death) X
area > 10cm2 خوف absorption
ulceration & Bleeding

. Less effective in dry surfaces: glans, Scrotum & labia

. Pregnancy [X]

Podophyllotoxin 0.5%
(مذيبة المنتقاة)

. purified extract of Podophyllin resin (the most active ingredient in it)
. So don't contain any of the ingredients responsible for toxicity of Podophyllin
. ∴ More effective > Podophyllin

يمكن كريم نفس اسم الكريم: Podophyllin Resin.

يطبق مرتين في اليوم لمدة ٣ أيام متتالية كل أسبوع لمدة ٤ أسابيع

. Pregnancy [C]
يسجل بطريقة الرضيع

---

3. 5FU
. → -- Thymidylate Synthetase enz → -- DNA Synth
→ -- Cellular Prolif. & Viral replicat =
. Limited data about Efficacy in genital Wart.
. ± used For: intraurethral Wart.
. Pregnancy [D]

4. TCA : used on Moist warts → Cautrized
Trichloroacetic Acid efficacy ?
. Pregnancy [C].
. 90% Conc.

(يصير كوي بسبب الرطوبة)

5. Imiquimod (Zyclara) 3.75% & 2.5%

- Mechanism: Immune response Modifier ?
  1. Act on Toll-like Receptors 7 & 8 on Monocytes & Macrophages → release of:
     - IL12
     - TNFα
     - IFNα
  2. ↑↑ APC
- preparation
  - Aldara: 5% Cream in 250 mg Sachet.
  - Zyclara: 3.75% & 2.5% C.
- Method:
- Efficacy: More Effective in Mucosal Warts > Warts on dry areas.
- S.E ①. Irritat.: Erythema, Erosion, Excoriation, Itching & burning.
  ②. Flaring of Ps
  ③. Hypopigm. (like Vitiligo)
  ④ Neuropathy
- C.I: Not recommended for ← intraurethral, Vaginal, Cervical Warts, rectal & intranasal
- pregnancy [C]
- children < 12 Ys → Safety & efficacy Not Known.

[6] IFN-α2b

. local inj. is better > systemic.

. SE: Fatigue, fever, Myalgia, Neutropenia, leukopenia, Flue like symp.

. Pregnancy C

. Children: can be used.

[7] Surgical Methods, for large reducnulation prefer Electro-, Cryo, Co_2 laser & Endoscopic surgery

↓

of Choice For Pregnant.

[8] others → Sinecatechins (Veregen)

. تستعمل بشكل موضعي فقط

. دهان ٣ مرات كل يوم

. لمدة ٤ أسابيع

(NB). 5 FU

1. Feat, Hyperpigmented lesion of Bowenoid.

2. intra urethral wart

↓

داخل الإحليل

Continous therapy

twice daily instillation of 5FU in the urethra

↓

irritation.

Intermittent therapy

twice weekly instillation of 5FU in the urethra

↓

. NO irritation

. تعطى مرتين بالأسبوع لمدة ٤ أسابيع

. تجنب الاتصال مع العين أثناء التطبيق

the of Choice For

. pregnan → Cryo

Non preg

1. Podofilox

2. Aldara

3. Sinecatechins

. For Children

. Cryo

. IFN α2b

. Aldara > 12

Vaccines in STDs

Which STDs have Vaccines?

- Some STDs, such as such as gonorrhea, Chlamydia, and syphilis, are caused by bacteria. They are usually effectively treated with antibiotics, although many patients do not know that they are infective and can spread the disease to other partners. The availability of treatments means that the need for vaccines against these diseases is not a top priority, although the increased resistance of gonorrhea to antibiotics may lead to a shift in priorities.

- Viral STDs are often highly persistent despite current therapeutic options or have no acceptable treatment available. Therefore, vaccines for certain viral STDs are in use, and others are in development.

Classification:
- **A) In use vaccines:** 1- HPV vaccine, 2- HBV vaccine
- **B) In development vaccines:** 1- HSV Vaccines, 3- HIV vaccine

1. HPV Vaccines (Emed. 2010)

2 Types (FDA 2006)

- (Gardasil)® (HPV4)
  - against 4 types of HPV (6, 11, 16 & 18)
- (Cervarix)® (HPV2)
  - Against 2 Types of HPV (16 & 18).

- Composition: Virus like particles consisting of recombinant L1 proteins from HPV (4 Types in HPV4 & 2 Types in HPV2) [Protein without DNA]
- Administration:
  - Gardasil: for ♂ & ♀ 9-26 ys (recommended Age is 11-12 ys but can be started as early as 9)

. Cervarix: approved for ♀ 10-25 ys.

. Dose: 3 doses at: 1 day, 2 months & 6 months.

. Eufficay: . are more effective before inf. & less effective after inf.

. in randomised Controlled Study involving 17622 women Aged 15-26 y →:

. ↓ Genital wart by 62%

. ↓ High grade cervical neoplasm by 19%

(in vaccinated versus placebo)

. Cancer أكثر سرطنة من الـ Wart

2. HBV Vaccines:

. Def: recombinant DNA vaccine Composed of HBs Ag protein → Anti-HBs Ag Formation

. Dose: 3 doses at: 1 day, 1m & at 6 ms.

. Recommended Populations:

The FDA has licensed several Hepatitis B vaccines for use in the United States. It has been part of the routine childhood immunization schedule since 1994. Following are the general recommendation for use of the vaccine:

Hepatitis B vaccination is recommended for all children, starting at birth in a three-dose series spread over many months. Additionally, all children and adolescents under age 19 who have not been vaccinated are recommended to receive the vaccine, as are adult populations at risk of HBV infection.

B- Indevelopment vaccines

1- Genital herpes vaccines:

- Vaccines for HSV are undergoing trials. Once developed, they may be used to help with prevention or minimize initial infections as well as treatment for existing infections.

Vaccines undertrials:

1- One vaccine that was under trial was Herpevac, a vaccine against HSV-2. The National Institutes of Health (NIH) in the United States conducted a phase III trials of Herpevac.[35] In 2010, it was reported that, after 8 years of study in more than 8000 women in the United States and Canada, there was no sign of positive results against the sexually transmitted disease caused by HSV-2.

2- A laboratory at Harvard Medical School has developed dl5-29 (now known as ACAM-529), a replication-defective mutant virus that has proved successful both in preventing HSV-2/HSV-1 infections, and in combating the virus in already infected hosts, in animal models. It has been shown that the replication-defective vaccine induces strong HSV-2-specific antibody and T-cell responses; protects against challenge with a wild-type HSV-2 virus; greatly reduces the severity of recurrent disease; provides cross-protection against HSV-1, and renders the virus unable to revert to a virulent state or to become latent.[37] His vaccine is now being researched and developed by Accambis (acquired by Sanofi Pasteur in September 2008), and is due to be applied as an Investigational New Drug in 2009.[38]

3- A private company called BioVex began Phase I clinical trials for ImmunoVEX, another proposed vaccine, in March 2010

NB. For HSV ...

Recent: genetically engineered growth defective HSV Mutant vaccine was designed to induce Th immunity by deleting ICP10PK (The Polarizing Gene)

↓

- ↓ recurrence 37.5%
- ↓ severity & ...

Types: 1. inactivated whole virus vaccines
2. live attenuated
3. DNA preparations
4. genetically engineered Mutant HSV vaccines.
5. Recombinant viral subunit vaccines:

- Glycoprotein B/D & the adjuvant MF59 → ...
- Glycoprotein D & adjuvant Monophosphoryl lipid A Immunostimulant → ...

Glycoprotein D Type

effective:

(1.) -- inf. in 40% of sero-ve women for HSV1 & HSV2

(2) -- symptomatic Acquisition in 70%

(3) Not effective for Men.

2. HIV vaccine

- Progress toward an HIV vaccine has been slow since the virus was isolated in 1983.
- Only three HIV vaccines have been tested in clinical efficacy trials. ***It is difficult to make a vaccine for HIV for several reasons:***

1. HIV mutates, or changes, much more rapidly than most other viruses. Targeting a vaccine to a rapidly changing virus is challenging task for vaccine researchers.
2. HIV damages the cells of the immune system. But to be effective, a vaccine must trigger the immune system to fight the disease agent. So, a challenge for HIV vaccine researchers is to develop a vaccine for HIV that must interact with the immune system in a way that is very different from the natural behavior of the virus.

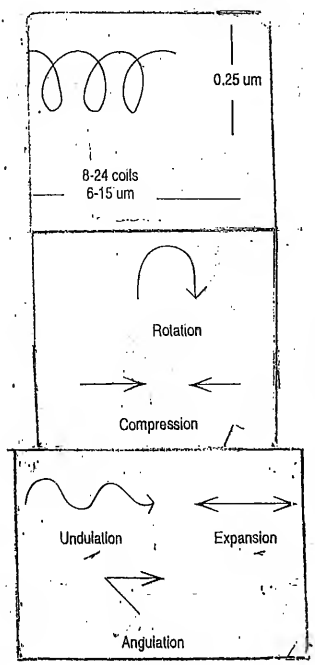
To date, researchers have developed several candidate HIV vaccines, but none has performed well enough in clinical trials to be approved.

< in use
in clinical
HIV HSV

Syphilis (S)

Q pathogenesis & MIC stages

- Def: chr. Infectious STD. That can affect any organ Except Ovaries.
- Aet: Spirochaete ~ Treponema Pallidum ; Gram -Ve
  - ... Spiral shaped bacteria with. [Biology]
  - very weak
  - highly infectivity 16-50%



- length : 6-12 um
- Width : 0.12-0.24 um
- Coils : 8-24 regular coils.

- Movement:
  - Locomot= [Corkscrew] الشكل
    - Compression
    - Expansion
    - Angulat=
    - Rotat=
    - Undulat=
- Multiplicat= : Transverse fission. (/33 hr)
- Mic Exam :
  - EM (Replp)
  - Conventional LM
    - Can't bee seen (< level of resolut=)
    - Stain (very thin)
      - Silver → dear brown
      - Giemsa → faint pink
      - Immunoperoxidase
      - IF
  - Dark ground (Field) Mic (DGM)
    - Luminescent against dark Back ground & chic Movement

T. Pallidum
order: Spirochaetes
Genus: Treponema

• Culture: . Not Cultured on artificial media (because they are obligate parasite)
. Can be kept for very short time on TPI medium.
. Non Pathogenic T. → Can be Cultured on artificial Media.

• Inoculation: Intratesticular or ID in Rabbits / Hamster

• Viability: destroyed by Heat (Drying & Antiseptics.) Soap water can remove it

• Immunity:

Natural
. there is Species-Variety Toward infect^
Rabbit is the only (primate) that can be infected by it.

Acquired (Syphilis-1921)

HI CMI
Chancre Immunity
local
. develops 2 wks after appearance of chancre
. if reinfect occur before development of this immunity → Multiple chancres.

(CMI)
Seen in 1ry & 2ry stage
(Perivascular infiltration of Monocytic Cells)
Plasma Cells, Lymphocytes

HI humoral
IgM → predominate in early stage
IgG → in Late stage (als. 1ry & 2ry)
IgA → 2ry & 3ry

NB Other Spirochaetes:

Pathogenic
. T. Carateum → Pinta
. T. Pertenu → Yaws
. T. Endemicum → Bejel.
. Borrelia vincenti & balanitidis.

Non Pathogenic
. T. Micro & Macro-dentum.
. Rieter strain.

These other Treponemes are BY!
. Similar Morphology To T. pallidum
. Cause different lesions
. Antigenically different.

Mode of Transmission:

- Venereal (95٪) (STD)
- Non Venereal (5٪)
  - Direct
    - Kissing
    - biting
    - Breast feeding
    - Transplacental
  - InDirect
    - Contact ē infected (Towels, Cups, Secretion)
    - Blood Transfusion
    - Accidental Inoculat~ (عن طريق)

Pathogenesis (مراحل سريرية)

1ry Stage (Chancre)

T. pallidum inoculat~ → (through breaked skin) → local EAO & cellular endo/peri arteritis obliterans → Infilt → Tissue destruct~ (chancre) 1-2 wks → L.N → lesion painless

(EAO: End Arteritis obliterans)

2ry Stage

Blood dissemination (2ry), ē delayed establishment of Immunity → affect~ all organs

Latent

absent of symptoms/signs

d.t balance bet. Immunity & T. pallidum: (why) ± d.t

1. Ass. Immunesuppression (down reg. of Th_1)
2. T. pallidum ± protected From Immune system (sequester intracellular locali. d.t < Coating ē Host ± plasminogen.

3ry Stage (Gumma)

↑ delayed hypersensitivity reaction

d.t DHR against (Relatively) Few T. pallidum → Granuloma

Other Mech. : T. pallidum locally
- ↑↑ in : GPI & Aortitis
- ↓↓ in : Gumma, TD & IK.

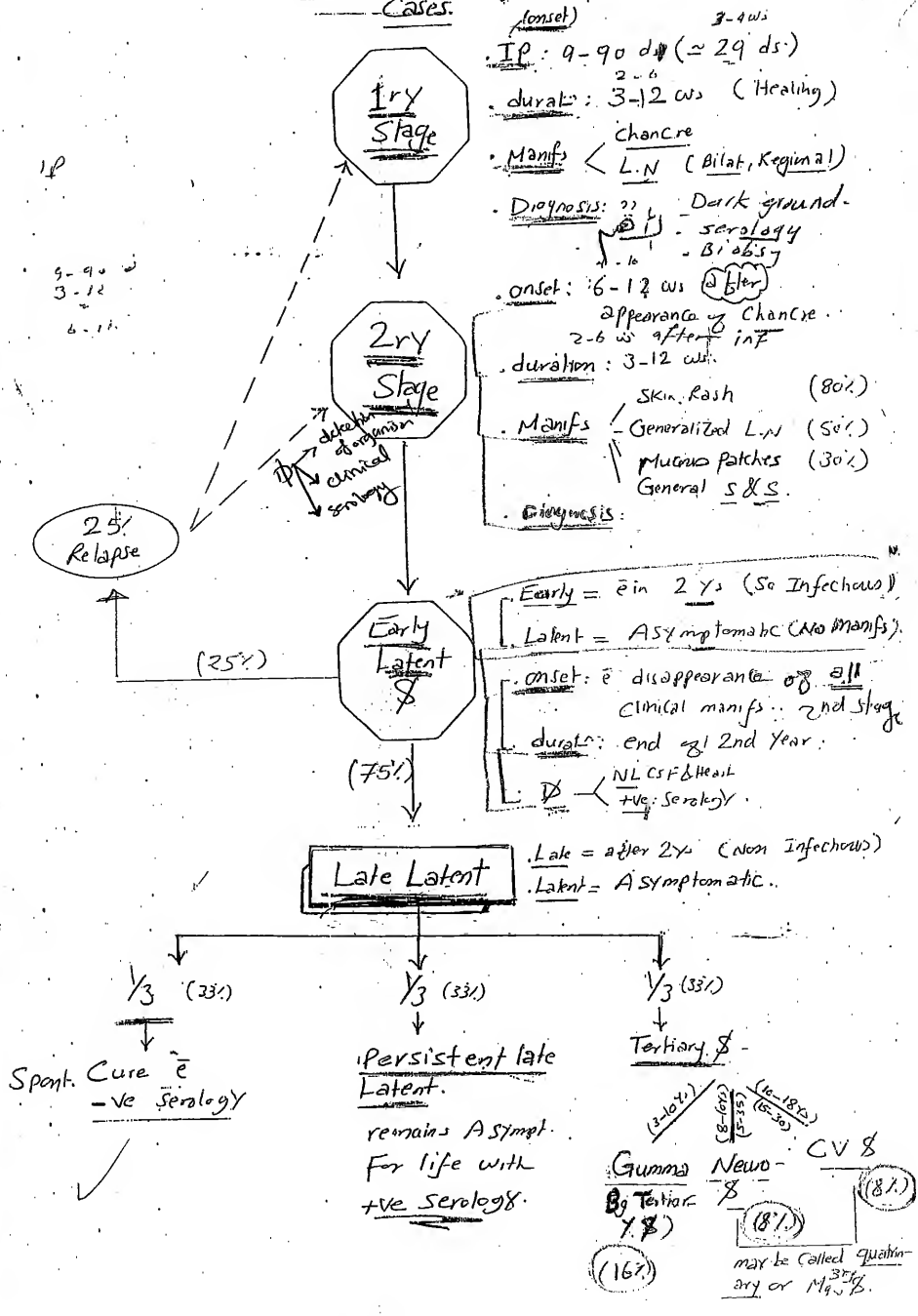
Types of ♂

- Acquired
  - Early (< in 1st 2 ys) → Infectious
    - 1ry Stage
    - 2ry "
    - Early latent
    - recurrent
  - Late (> 2 ys) → Non-infectious
    - Late latent
    - Tertiary stage (CNC)
      - Gumma
      - Neuro ♂
      - CV ♂
- Congenital
  - Early
  - late
  - Stigmata
    - permanent stears of ♂ lesions.
    - الى كانت موجودة عند الـ newborn

[early - late

Acquired S

- Natural Hx of untreated Cases.



1ry Syphilis (Chancre)

- Chancre starts as Papule → ulcerate.

Ulcer
اسمها بتاع اي
"ulcer"

Single painless indurated

- IP: 9-90 days (usually 2-4 wks 29 ds)
- No: usually single (why?!) ; rarely < absent / Multiple
- Site: it may be
  - Genital (95%)
  - Extragenital (5%) → anus, lips (Tongue), Nipple, areola.

Succumbs

♂
- glans
- Sulcus
- Frenulum
- Intra meatal

♀
- Labia <
  - Urethral &
  - Cervical (Concealed)

لازم (Concealed) → NGU & discharge.

- Size: 0.5 - 2 Cm
- Shape: Rounded or oval. مدببة
- Edge: Elevated & Sloping Towards Center (Saucer Shapped)
- Floor: Clean, pale-red, oozing (serous)
- Barge: Indurated. (like button (in) tissue). زي الزرار
- Tenderness: Painless.
- Fixed: → Not fixed.

Seen / Not felt
Felt Not Seen

انصح بـ
مواصفات
- Single
- Painless
- indurated

L.N (after 1-2ws) — Enlarged, not tender, Mobile, rubbery, Normal overlying skin, discrete

Bul: Bilat: in genital lesions; unilat: in Extra genital "

Fale: Slow Healing within (3-12ws) by SCar: Thin, Atrophic, non-contractile.

NB

Clinical Varieties of Chancre:

1. Absent Chancre: ± d.t.
   - Healed
   - Concealed < Intramuscular, Cervix
   - deep inoculation e.g. Puncture.
   - Blood Transfusion (also ...)
   - Follman Balanitis
   - Cong. ♂
   - Chancre Immunity
2. Multiple: Multiple Infection within 2ws
   - Kissing: Contagious surfaces: Scrotum ⇒ Thigh.
   - 2ry bact. Inf (Common in HIV Pts).
3. Painful: if < Jarisch Herxheimer React⁻ (Combustion, Toxine)
4. Condom Chancre → at base of shaft.
5. Combined (mixed): Coinfect⁻ ē H. Ducreyi, hemophilus → (Painful)
6. Phagedenic: Super Added inf. by < Fusiform bacilli, Anaerobic, Spirochaetes → Severe destruct⁻, sloughing, Gangr → scarring.
7. Chancre redux (relapse): Chancre developed on Top of Scar of previously Healed Chancre.
8. Pseudo Chancre Redux → Gumma develop on Scar of Healed Chancre.
9. Edema Indurativum: Chancre + Severe Solid edema
10. ♂ balanitis of follman: Extensive Circinate or Erosive balanitis ē No chancre.

Chancroid (T.P) — inject whole contents of pus if it is thick

Absent
Multiple
Painful
Phagedenic
Condom
Combined
Redux
9, 10
Bubo: decide

NB2 • No L.N (Bubon d'emblee) if:

① Blood Transfusion (Congt طريق انتقال (Transplacental)) ← (No < Chancre / L.N = No 1ry stage at all).

② Concealed Chancre in Cx: → draining to deep iliac L.N.

③ Cong. ✗ (No 1ry stage at all).

NB3 • 25% of chancres are Atypical → Multiple, Painful, 2ry bact.

• DD: ✗ chancre → Causes of Genital ulcers. (دي تناسلية)

• Diagnosis of Chancre: < 2 Mum Inv. / 4 other Inv.

① Dark ground Mic (or DIF): → "Only sure Method For Ø" [2.5-92% sensitivity]

↓

the material for examinat° is either from the ulcer or L.N.s ← no ص

In order to Remove: Scab ← Red in dead organic matter e.g. Fusiform bact. / Saprophytic organisms (B. regringes, B. Balanitides)

Firstly: Clean the ulcer (gauze soaked Saline or water) & give 1 gm Sulphonamides / 4 times/d (يشتغل T.P to guard against Sepsis also has adverse. of non Treponemicidal).

Aspirate from L.N

* Indications:
→ ① -ve ulcer inv.
→ ② if ulcer is treated by antiseptic applicat°
→ ③ hidden or concealed ulcer.
→ ④ Mouth chancre (ليش؟ Why??)

NB (DGM) → Not done for oral lesion d.t Presence of Non pathogenic Treponema (T < Micro dentium / Macro ") → False +ve (لأن الجراثيم هاي)

② Serological Tests : +Ve in (60%) of Cases (+ve 2wks after appearance of Chancre)

③ Other Invs

[A] DFA-T.pallidum test : Direct fluorscent antibody
- Done on Fixed smear
- Diagnose oral lesions (oral Chancre)

[B] PCR

[C] Intradermal TP Color test : IV Evans Blue dye → Then Inject Killed "Nichol Strain" ID → Color Spot at inoculation Site.

[D] Biopsy → Indication → "In HIV Patients"

Why?? because of Abn L Serological Tests (w) may be < very High / low / Fluctuating

In all S lesions Biopsy Findings include:

① EAO (at 1st: Endoth. Prolif.: T. pallidum)
- T. pallidum attach to Endothelium → EAO → Heal by Scar (obliterate)
- ابي لمفرنيتيه وبيبه هيدوشغ ابي رض تاني

② Plasma Cell-rich mononuclear Infiltrate [perivascular infiltration of Lymph. Plasma. Mucosa]
- in S → Early
- Other dis. → Late.

NB: Chancre HIV → Painful / Biopsy (VV) For B

2ry Syphilis

def: Stage of Generalization of ↓ d.t Blood dissemination, it affects the whole body From Hair To Toes Except ovaries.

Onset: 6-12 ws after appearance of chancre (chancre: may be healed or going to heal)

2-6 w after appearance of inf. (25% of Cases start with presence of chancre).

duration: 3-12 ws → then → Early latent

Manifs: ① Skin Rash (80%) ② Generalized L.N (50%) ③ M.M le sions (30%) ④ General Manifs

Etiopathogenesis: Blood dissemination of T. pallidum

Skin Rash (Syphilid) (80%)

(يظهر بشوفه عليه Day light)

P-R مع تركيب pit Rosen

تكون بس اذا ↓ PR PLEVA EM DE

General Ch

- Generalized, Bilat & Symmetrical
- More common on Flexors / Flanks & Trunk (pp: أسفل الجذع والأطراف السفلية)
- Polymorphic & Coppery red.
- Never: Itchy → Except (Lichenoid & Condylomata); Vesicular; Scarring: but± Post. Hyperpig. / Leucoderma colli: (Hypopigm.) residual depigmentation Surr. by Hyperpig on The Neck Specially in "Brunettes" (إمرأة سمراء)

Types

- Macular
- Papular
- Maculopapular
- Pustular
- Papulosquamous
- Condylomata lata.

no vesicles ↓ presence of vesicles ↑

Types of The Rash: (Commonest is Maculopapular):

(1) Macular (Roseolar) Syphilid:

Macules: Rounded, 0.5-1 cm, Rose pink.

(2) Papular Syphilid: (Commonest)

Papules: Rounded, Indurated, 0.5-1 cm, Dull red

Variants of Papular Syphilid:

- Annular
- Follicular → at scalp → Moth eaten (Alopecia)
- lenticular → Lentils like
- Lichenoid → L.P like.
- Corymbose: large central papule surrounded by smaller satellite papules
- Corona Veneris (Crown of Venus): lines of papules on forehead below ant hair line.
- Biett's Collarette: ring of scales surrounding a central papule.

NB: PP lesions Ck By

+ve Ollendorff's Sign: Papules are Exquisitely Tender to touch of a blunt object. [They are very common & clue For ✗]

(3) Papulosquamous Syphilid:

large scaly papules & Plaques (Psoriasiform)

(4) Pustular: d.t EAO (Marked) → Central Necrosis → pustules

Types:
- small acuminat
- Large
- Flat
- "Pustulo-ulcerative" (Rupial or Oyster Shell Syphilid)

Black-brown Crusty lesions:
Ck By: (1) More in face
(2) " Immune Compromised
(3) " ass. w Neuro ✗

⑤ Condyloma latum = Moist Papules

Most infectious lesion ✓ (High No. of T. pallidum)

- lesion → عدد
- Site: Moist opposed areas & Mucocut junctions
  - Axillae & groin
  - Perianal
  - Genital
  - Buccal cominsures

Condylomata lata	Condyloma Acuminata
→ T. pallidum inf.	→ HPV inf.
Flat & Sessile	. Cauliflower & pedunculated
. Surface: Smooth / Moist	. Rough (Verrucous) / Dry
. Color: dull red Flesh or greyish-white	. Skin Colored.
. Base: Indurated	. Soft
. Doesn't Bleed easily	. Bleeds Easily.
→ Moist opposed surfaces	. Genital only.
→ Invs: DGM +ve / Serology +ve	. Both −ve → Clinically D
→ (IM) Penicillin	. Podophyllin not in pregnant women

. Framboesiform Syphilides: Eroded lesions on intertrigenous areas ē may proliferate → large, elevated, brown-red Crusted Patches ē dried Serum.

. NB: DD syphilid From Drug-Eruption:
- ↓Hx
- ↓Rash
- ↓No L.N

Any pt ē generalized Dermatitis + L.N → Consider 2ry S.

ايه هو الـ 2ry الى شكله يشبه (2ry S) بالضبط !!

P. Rosea

② Generalized L.N (50%): As before

- Firm, discrete, Non < Tender / adherent

Generalized L.N e.g. cervical, occipital, axillary, epitrochlear.

③ Mucous Patches (30%)

- Start as papules or grayish white
- ∴ Patches → sloughing & ulcerate →

i.e. "Snail Track Ulcer" or Serpiginous ulcer

∃: Tonsil, Tongue, Nose, oropharynx; Mouth angles, CX, anus.

dorsal Tongue lesions called: "Plaques fauchees"

in ② mucous patches are:

- Smooth
- rounded
- dull pink
- destroyed filiform papillae by Necrotic process.

"2ry"

Malignant ⅋: rare Form of ⅋ Ch BY:

(⅋ Maligna Praecox)

① Toxemia & fever ass. ē deep ulcerating lesions That may → death.

Severe ② oral ulceration & mucous patches.

③ -ve serology

④ More likely to develop Gummata.

(4) General Manifestations

1. Constitutional Manifs : FAHM & anemia
2. CNS → meningitis with Cranial Nerve palsies
3. Eye → . Uveitis . Chorioretinitis . irregular pupils.
   . Iridocyclitis . Punctate Keratitis.
4. Resp. → . Hoarseness of voice (d.t ulcerative & Edema of Vocal Cords).
   . Cough : Bronchial Mucous patches.
5. GIT → . Epigastric pain
   . Nausea
   . diarrhea.
6. liver → Hepatitis, Jaundice & megaly [C/P → similar to HCV ↑ APK. disproportionate to Transaminase Rise.]
7. UT → ♂ nephritis
8. Ms → Myopathy
9. Joints → arthritis & Effusion.
10. Bones → . Nocturnal osteolgia . Periosteitis ← Skull, Ribs, Sternum "Commonest osseous manif."
11. Hair → 2 Alopecia Types "♂: ↓ hair loss in ♂"
    - Diffuse ± d.t.:
      1. TE (in 3-5ms).
      2. Jarisch Herxheimer reacts
    - Patchy → Moth eaten Alopecia at Sides & back of Head
      ✓. Nevere → Complete
12. Nail → onychia & Paronychia.

. Diagnosis of 2ry ♁ (lip.sp)

(1) clinical
(2) DGM For ← Mucous Patches (No swab) / Condyloma lata
(3) Serology (100% +ve) → Except ← Prozone phenomena, Mg & HIV (so Biopsy)
(3) Biopsy ← as chancre but less intense lichenoid . perivascular plasma cells - granulomatous

Latent S

Early latent S

- 1st 2 yrs
- infectious
- Asymptomatic
- +ve Serology
- 25% Relapse.

- onset: after disappear of 2nd stage
- duration: after 2y
- AIE: → dt balance
- SIS → absent.
- Dx: CXR, Echo, Serology

Late latent S

- occur after the 2nd year.
- non infectious.
- Asymptomatic (discovered accidentally during donation or premarital test)
- +ve Serology
- No Relapse.

- Is danger not d.t infection but the possibility of Neurological or Cardiovascular Complications

So the following should be done:

*. invs for < CV & Neuro S (By)

① CSF

② CXR & Echo (S Aortitis)

③ "Quantitative" VDRL or RPR

"positive" if they Reactive

Relapses In Early S

Dx 25% of S patient will relapse within The 1st 2 yrs (Early latent)

Types of Relapse:

① Clinical Relapse: < Recurrence of 2ry S. or " of Chancre (Chancre redux)

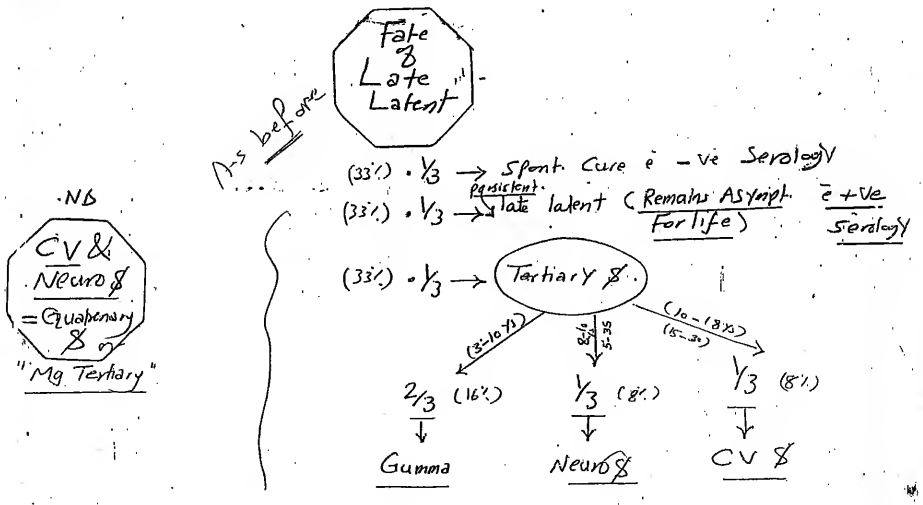
② Serological : Change of Reactivity (Sero -ve become sero +ve or sero +ve show ↑ titer, after Rx)

③ Transplacental: apparently Cured Mother with < Birth of S Child / Infect of Her Sexual contact

How to differentiate bet: Chancre Redux & re infect ?? (Redux should After)

Late (Tertiary) S

Def. • Late: after 2y. Sa → non infectious • Latent: Asympt.



• Late S is Cx By → Specific tests: +ve; Non " " : (may be -ve.)

Benign Tertiary (Late) ✓ "مرحلة ثالثة"

(Gummata) = Granuloma caused by DHR against relatively low No. of T. pallidum.

Any site can be affected but commonest is:

- Skin
- MM
- Supporting Structures (specially Bone). Joint - MS.
- Visceral organs

Gummata of Skin — def. Deep granulomatous process of Dermis & S.C.T. ~~but~~ involving Epidermis secondarily.

(4 Varieties)

(1) Nodular/Noduloulcerative:

- rounded dull red at any site of skin.
- Single or Localized in groups ē "Poly Cyclic edge"
- Painless (painless Asymptomatic nodules)
- Fate either:
  - ulceral → Punched-out ulcer
  - Healing ē scar → thin - atrophic (tissue paper)
  - // ē Pigmentation

(2) Squamous / Psoriasiform lesions:

- Palmo-plantar large Nodules covered ē Waxy Scaling (Similar To Ps. but No Auspitz Sign)
- There may be central Healing.

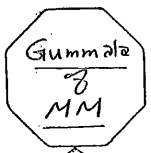
(3) Subcutaneous lesions: (Most Common):

- rounded, painless, S.C. Swellings → ulceration → Gummatous ulcer. (Vertical)
  - Edge: Punched out ē Poly Cyclic bodder
  - Floor: dull red GT & Wash-leather sloughs (Tough yellowish white sloughs).
  - Base: Indurated
  - Pain: Painless.
  - L-N: No L-N (Painless L-N Fixed)
  - Fixation: may be fixed to underlying Structures

Wash = غسل

- Edge: → peripheral Extension → plaques with polycyclic or Arciform border.
- Site < usually: upper & outer legs (pretibial).
  (Trauma sites) < may be: scalp, face, sternum buttocks.

④ Pseudo-chancre Redux: Gumma appears at site of previous chancre.



Localized:
- Painless, swellings & Nodules → break down → punched out ulcer
- Site: Nose / Mouth < Uvula, Tongue / Larynx & pharynx
  ↓ painless nodules → ulceration → ① Perforation of Nasal Septum & Hard Palate → "Saddle Nose"
  ② Destruction of Uvula → Nasal food Regurge.
  ③ Stenosis of Pharynx → Hoarseness & Larynx → Dysphagia.

Diffuse:
- NB
- Tongue: may be involved in all stages of S:
  - 1ry → chancre
  - 2ry → Mucous Patches
  - 3ry → Gummata
  all forms are precancerous so follow up after H For Mg.

④ Tongue: affection by Gumma may be:
- A. Localized → Painless swellings → punched out ulcers
- B. Diffuse → 3 clinical varieties:
  (i) Scrotal tongue: Deep irregular Fissures [d.t. interstitial Fibrosis].

(ii) Leukoplakia like: irregular white patches on surface of Tongue → Pre Cancerous

(iii). Chr. Superficial Glossitis: Smooth, red. glazed Tongue: d.t loss of filiform papillae → discomfort & pain.

- Bone
- Joint
- Cartilage
- Ms → Contracture & Joint Fixat^ (d.t extension From Bone).

Cartilage: perichondritis of Costal Cartilage & ear.

Gumma of Bone

2 Types:

Syphilitic Periostitis

Syphilitic Osteomyelitis

Long Bones

- subperiostal inflamm & Infilt. → new bone format^ → irregular surface (without Fracture (on the convex middle of Tibia → Sabre tibia))
- Symptoms: No Fracture But: Nocturnal Ostalgia.
- XR: ↑ Cortical opacity & Sabre tibia (thick ant. Border of tibia).

Gumma of Joints (Uncommon)

- Arthralgia, Arthritis, Synovitis
- Knee joint → Swollen - rubbery .. No signs of Inflamm.
- Site: Joints of Stress (Knee & Elbow)

F Pat → osteomyelitis

Bones e.g. skull, ribs, nasal septum

- Medullary inflamm. & Cellular Infiltration → (No) new bone formation → Pathological fracture. ✓

(Post fracture)

- X-ray: → Worm Eaten appearance. (rounded Areas of Bone loss)

Gummata of the Viscera. (Comment fr liver)

- liver
  - Diffuse Gumma: → diffuse interstitial Cirrhosis (Form of Portal Cirrhosis)
  - localized " : → Irregular Fibrosis (Hepar lobatum)
- Stomach
  - Diffuse
  - localized → "leather bottle stomach" (w/ pylorus)
- Respiratory
  - larynx: → Hoarseness & aphonia
  - Lung:
- Testis
  - localized: ass ē Ant scrotal skin ulceration (DD: Skin TB spread dt hematogenous post)
  - diffuse: diffuse painless Enlargement ē lost Sensation (Billiard-Ball testis) كرة البلياردو

Hepar lobatum
leather Bottle Stomach
Billiard Ball Testes
Ant scrotal ulceration
PCH
Donath-Landsteiner reaction

Liver of Liver

Hepar lobatum

respond to H but therapeutic paradox may occur.

Billiard Ball Testis

- Heavy
- Painless
- Smooth
- unilat
- ± Hydrocele.

Blood

PCH = Paroxysmal Cold Hemoglobinuria. (2ry To TB epididymitis)

- Def: Form of Hemolytic anemia that may be rarely associated with late S (Cong. or Acq.)
- AE: dt presence of (Hemolysin) ē combine ē RBCs during Cold Exposure → (Sensitized RBCs)
  - on rewarming: Sensitized RBCs destructed by Complement
- CIP: FAHM, dark urine & jaundice.
- D: Donath-Landsteiner reaction.
  - Chilling of Blood Sample → rewarming in presence of "C" → Hemolysis.
    - "Complement"

Diagnosis of Gummata
(Bg Tertiary ✓)

1. C/P & Rad.
2. Histopathology
3. Serology (+ve)
4. CSF Exam ✓
5. CXR & Echo.

DGM

Q: DGM for Gummatous lesions??
↓
Very low no of organism ✓ ✓

Neuro ♁ H4 (باسم يا)

- Incid: 8% of untreated ♁ patients.
- onset: 8-10 ys after Inf.
- NB: T. pallidum can be found in CSF (4-24%) From time of chancre appearance. (CNS affect ↑ can occur in Any Stage of ♁ even Early).

Classification: T. pallidum may affect:

1. CSF → Asymptomatic Neuro ♁
2. Meninges → Meningeal Neuro ♁.
3. BVs → Vascular Neuro ♁
4. Parynchema → Parynchematous Neuro ♁.

① Asymptomatic Neuro ♁: (Latent Neuro ♁)

dg: Abnl CSF in absence of Neurological S. &S.

+ve CSF changes: 4

- Lymphocytes ≥ 5/HPF
- Protein > 40 mg% (IgG & IgM)

Most Sensitive Indices & 1st to return after treat ♁

- +ve Serology For ♁ — Specific / non specific (in) Serum & CSF
- +ve Colloidal Gold test (Lange test): ← Globulins
  - in ♁ The A/G ratio shows Predominance of G.
  - Colloidal Gold Sol is ppt. by Globulins, projected From ppt. By Albumin.
  - serial dilutions of CSF ($\frac{1}{10} - \frac{1}{5120}$) + 4 ml Colloid Gold Sol.

→ Asso degree of ppt. From the Color of the Fluid:

Results
- 0-1 → NL
- 2-5 → AbNL

- ⓪ → Red rose (No ppt)
- ① → reddish Blue
- ② → Lilac or Purple
- ③ → Blue
- ④ → Colorless, Trace of Blue
- ⑤ → Colorless (complete ppt).

NB This test reflects Changes in CSF protein & Not specific Test For ✠.

- Classification of A Sympt. Neuro✠:

1. Type I
   - Cell & protein changes → minimal
   - Reagin tests → -ve
   - Lange test → NL Curve.
2. Type II
   - Cell & proteins → ↑
   - Reagin tests → weak +ve
   - Lange test → mid Zone
3. Type III
   - Cell & protein → ↑
   - Reagin → Strong +ve
   - Lange → 1st Zone Curve.

↓

مرحلة لازم متكمل لتحول GPI لـ

- Fate of Asymptomatic Neuro✠: either

① Spontaneous resolution في

② progression To Symptomatic Neuro✠. (this يكمل Called Red Flag of Stokes) وقاد لتاي

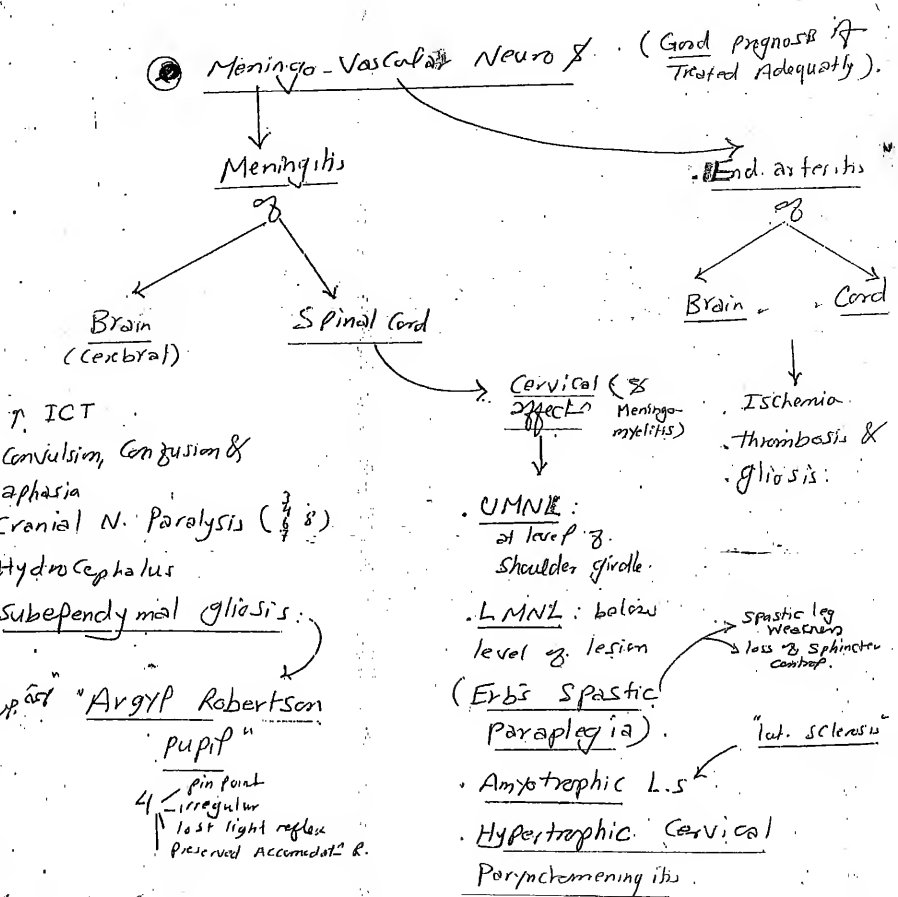
- Indications For CSF Exam:

- ## ① 2 yrs after ## of Early ✠ (to exclude Asympt. Neuro✠)
- ② Serological Relapse & Serorelapse result. after ## of Early ✠
- ③ if There are Neurological SKS
- ④ HIV patients. (High Incid of Neuro✠).

إذا بيكمل علاج وسن بيخف.

Table 10.1: Classification

Asymptomatic	*No signs/symptoms*	*CSF changes only*
Meningeal	Cerebral	Acute, subacute or chronic meningitis affecting the vertex or the base of the brain
	Spinal	Hypertrophic cervical pachy-meningitis, doisolumbar meningitis and amyotrophic lateral sclerosis
Vascular	Cerebral	Syphilitic vascular thrombosis leading to various syndromes depending upon arteries involved.
	Spinal	Syphilitic vascular thrombosis leading to paraplegia below the level of involvement.
Parenchymatous	Cerebral	General paralysis of insane.
	Spinal	Primary optic atrophy. Tabes dorsalis.
Gumma	Cerebral	Symptoms and signs of space occupying lesion.
	Spinal	Symptoms and signs of space occupying lesion.



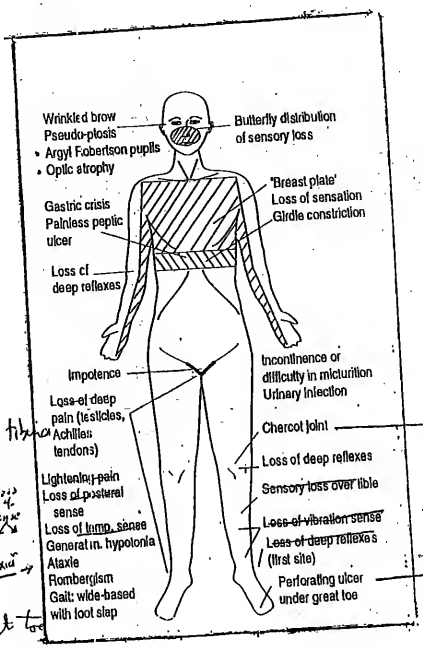
Parenchymatous Neurosyphilis

Any of Parenchyma may affect

- Spinal Cord (dorsal < Roots / Columns) → Tabes dorsalis
- Cerebral Cortex → GPI
- Both < Cord & Cortex → Tabo paresis

Tabes Dorsalis

(Tabes = degen. or wasting)



- wrinkled brow
- Pseudo ptosis
- Argyl Robertson
- optic atrophy
- painless, gastric ulcer
- gastric crisis
- Loss of pain
  - postural sense
  - temp sense
  - vibration sens
  - deep reflexes
  - sensory loss at tibia
  - ~~bigger~~ sensory loss (Butterfly) sign
- Hypotonia
- Ataxia → Ataxia
- wide based gait
- perforating ulcer under great toe
- Incontinence
- Hypotonia

enlarged, Nc eff. / Hypermobile, deformed → dislocate & Fxs

Indolent, Circular, painless

Diagnosis

- Serum: VDRL / RPR / TPHA / FTA ABS
- CSF: Cells, Protein, Sugar, VDRL, Gold sol curve
- Lange test: GII (Luetic) Curve
- Reagin test: 25% −ve
- FTA ABS: 95% +ve

General Paralysis of the Insane (GPI)

def: Progressive parenchematous dis. of the brain that produce
1. physical & mental deterioration
2. complete dementia.
3. Paralysis
4. Incontinence

+ "Hand writing"

onset: 10-20 yrs after Inf.

C/P:

Symptoms	Signs
. Intellectual impairment	. Tremors of Tongue, Hand
. Failed memory	. Abnl. pupils
. ↓ Concentration	. Dysarthria
. ↓ Judgement	. Convulsions
. Delusion	. Incontinence
. Dementia	. pyramidal signs
. Mood changes.	

Pathology

. dura Matter → Thickened & adherent to skull
. Pia Matter → " & " to Cortex
. MIC. → . perivascular infilt. of Arterioles & meninges
. Iron containing Histiocytes (Microglia) ↓ Pathognomonic

NB on GPI

· Exam. of patient:

1. Mental status → deterioral ↑
2. speech → dysarthria, hisitancy & slurring
3. ocular (Pupill) Changes:
   - Commonest sign in GPI ✓✓
   - Argyll Robertson pupil
4. Hand Writing:
   - Misspelling of < words omissions
   - Misplacements & repitihons of Letters & Syallables.
   - (Agraphia) in Late stages
5. Face: - Expressionless
   - Flattening & Smoothening of Nasolabial Folds
   - Tremors of lips & Tongue.

اختبار الكتابة بمريض

Thomas Rodrigues
Afonso Pairo Bardes
Goa

Tomas Rodrigues
Moura Bardes
Goa

Fig. 10.1: Handwriting of GPI

Diagnosis: - Tange Type III
- VDRL (CSF) +Ve
- EEG +Ve (↑>50%)

Cardio Vascular ✗ (CV ✗)

HU (المحاضرات) (محاضرة أزهرية) 2006

- M : F = 1 : 3
- 40% are Neuro ✗

- Incid : 8% of untreated ✗.
- onset : 10 - 18 ys.

- Classificat° : it may affect : (1) Heart
  (2) Medium Vs ← Cerebral, Carotid, Hepatic
  (3) Great Vs .. (Aorta)

legs.

- Heart (rare)
  there ±
  - local 2nd affect (Isumma) → HB
  - diffuse affect of Myocardium → HF

- Medium Vs (rare)
  there may be.
  - destruct° of elastic layer.
    - NB Aortic Aneurysm
      - Ascending
      - Arch
      - descending
  - Intimal prolif.
    → Pathological Narrowing of:
    1. Cerebral
    2. spinal
    3. Cardiac
    4. iliofemoral → leg pain.

(Vs)

- Great Vs affect° (Aorta) Activat. of

- the organism reach the (Vs) Via Vasa Vasorum in the adventitia (where) it excites Cellular infilt. of Plasma cells & Lymphocytes →:
  1. Adventia: → fibrosis & narrowing of Vasa Vasorum
  2. Media: → fibrosis & destruct° → Saccular aneurysm & ± AR (if extend to Aortic Ring)
  3. Intima: → destruct°, thickening & Calcified Patches → Coronary Osteal stenosis.

NB. Aneurysm of ✗ is saccular while of Asthrosclerosis is fusiform

CIP

1. Uncomplicated Aortitis (usually Ascending) → Retrosternal Pain or Asymptomatic.
2. AR → manifs. of RHF.
3. Aortic Aneurysm
   - Ascending: Aortic Systolic Murmur. ("Commonest")
   - Arch: → Mediastinal Synd
   - descending → Vertebral Erosion & low back Pain.
4. Coronary osteal Stenosis: Angina & death.

Diagnosis

1. CIP
2. X Ray & Echo
3. Serology (+Ve in 80%)
4. CSF (to exclude Neuro S).

NB:

Aortic Aneurysms

Ascending Ao. (+++) (An. & Signs)

Pressure on
- Rt lung → dullness by percussion
- Ribs & Mediastinum → Pulsating mass
- Trachea or Pulm. a → RHF
- Pericardium → Tamponade

Ribs, Sternum, Vertebra ← 3 Bones

Arch (+++) (An. & Symptoms) → Mediastinal Synd.

3 Tubes
- Trachea → Stridor
- Eosoph → dysph.
- Lt bronchus → Collapse & Hemopt.

3 Ns
- RLN → Hoarseness
- Symp. → Horner's Synd
- Phrenic N. → Paralysis of diaph.

descending Ao. (No S & S) → ± Back Pain.

Congenital ﷺ (Prenatal ﷺ) (سوال امتحان)

def Transplacental (Prenatal) Transmission of ﷺ
From Infected mother (usually during early ﷺ)
To the Fetus (after the 4th month).

يعني مرض ← Early ﷺ (1y, 2y & Early latent)
after 4th month (T. pallidum can't cross the placenta (Except after 4th month).

الجراثيم التي تنتقل transplacental تكون باقي او مراحل

Note: Infect° is Transplacental & In contrast to Gonorrhoea, Chlamydia & Hsv ↑ &HIV. occurs Intra partum (Vaginal delivery) → So. → No 1y stage (Blood borne Inf.)

Intrapartum (Cx thanch)

ﷺ & pregnancy:

A. Effects of ﷺ on Pregnant Mother: Benign (Same effect as in non-pregnant)
Fetus:

1. Abortion after the 4th m.
2. prematurity
3. Still born (macerated fetus) ﷺ at time of delivery
4. Cong. ﷺ either NL then develop ﷺ (usually 3ws-3m) occur later on.
5. Healthy child

Hyic bullae (Large NB 2 TP) Macerat° Protuberant Abd + HSM

6. placental ﷺ: placenta is bulky; Heavy, Greasy & pale; Large No of T. pallidum.
7. Kassowitz law: better prognosis occurs in successive pregnancies [d.t prolongation of period from the date of Maternal Inf.]

كل ما كانت الحمل كل ما كان لديك تأثير على الجنين أقل

Risk of Infection:

1. Conception → 7th m → 100% Transmission
2. 7 & 8ms → ↓ risk
3. 3-6 wks before delivery → No Transplacental Transmission but may be "Intrapartum"

B Effect of ✗ Infant on the mother:

(Colle's Law): ✗ Infant doesn't Infect the mother who is already Infected & has a degree of Immunity.

3 Laws
- Kassowitz
- Profeta
- Colles.

Profeta law:

because the baby may be born healthy & then develop Syphilis after (ws - ms), So: one should depend on investigations of Blood Sample taken from umbilical Vein Acc. to "Profeta law":

(NB) Results of umbilical Vein sampling may be:

- False - Ve (doesn't Exclude Inf.) → So Follow up for 3 ms For development & Later on.
- False + Ve → d.t passive Transfer For Abs From the mother → So
  - look for VDRL Rising titer (Diagnostic) "الدائم"
  - or FTAAT (IgM) (IgM doesn't Cross the placenta)

[Inf. = نقل المرض]

good ✗ of Mother
- Before 4 ms → Prevent Infect^
- after 4 ms → In utero cure doesn't prevent.

affect^
- Bone Joint
- Neural degen.
- IK.

IK
- deafness (Nerve)
- clutton's joint → (Hydroarthrosis)

→ ✗ Hypersensitivity React^.

Congenital Syphilis

Early Congenital Syphilis

- Early Congenital Syphilis (similar to 2ry Acquired Syphilis).
- Before 2 years of age.
- Infectious.
- "Usually" no primary stage because it is Blood borne infection but chancre may be occasionally occur from infected mother during Vaginal delivery.

A Rash as before + Bullous pemphigus Eruption (earliest Eruption = congenital pemphigus) (+) on the Alopecia Periorificial Fissures.

B Generalized Lymphadenopathy

C Mucous Patches → Rhinitis (Snuffles)
- of Nasal Mucosa
- → difficult sucking
- → Conductive deafness.

D General Manifestations:

1. Senile Facies: d/t dehydration (wrinkled face + CAL color of skin) hydrocephalus.
2. CNS: Syphilitic Meningitis ← stiffness, Bulging fontanelle.
3. CVS: "very" rare.
4. RS: may be fetal pneumonia.
5. Renal: NS or Acute Nephritis.
6. Lymphoid syst.: HSM & L.N R ± LCF.
7. Eye: chorioretinitis that manifests as Salt & Pepper fundus on exam.
8. Bones: 1st y: ± osteochondritis → ± Pseudo Paralysis (d/t painful swelling & epiph.)
   - 2nd y: ± dactylitis: of proximal phalanges → Fusiform Fingers.

Late Congenital Syphilis

- Late Congenital Syphilis (after 2 years) not infectious.

1. Clinically: similar to tertiary ± (Gumma) ± others:
   - 2. Hypersensitivity manif.
   - 3. Bones.
   - 4. Neuro:
   - 5. CV ±
   - 6. Blood.

2. Hypersensitivity manif: (3 itis):

A Interstitial Keratitis: the Commonest lesion, its hypersensitivity reaction that →
- ∴ Corneal vascularization: Salmon patch
- ∴ Cellular infiltration: Ground glass. (Hazziness)
- → on slit lamp ea.

B Cochlear Neuritis: Cochlear nerve inflamm.
- → Perceptive deafness
- N.B: Conductive deafness may occur d/t ± Rhinitis. in early stage of Congenital Syphilis.

C Clutton's arthritis: Painless effusion of Knee Joint
- (Little) impairment of Mobility
- Rad: enlarged Joint spaces (∵) no bone or Cartilage changes.

3. Bones:
   - At first: Bone formation
     - Skull: Parrot's nodes
     - Clavicle: "Higoumenaki"
     - Tibia: "Sabre tibia"
   - Later on: Bone destruction
     - Nasal Septum destruction
     - Collapse of lower part of Palate perforation

- Periostitis: onion peel appearance: ✓ → Subperiosteal new bone.
- Wimberger Sign: ↓ density of upper tibia. (earliest X-Ray sign).

2 Rad Signs

Stigmata of Congenital Syphilis

(مرض) Stigmata (Remainders) of Cong. Syphilis. (Permanent scars & deformals that result from the lesions of Cong. & persist for life).

Stigmata of Early lesions (B) (appear)

1. Salt & Pepper fundus: (Residual areas of pigm. & atrophy)
2. Saddle Nose: depressed nasal bridge

3. High arched Palate: (d.t improper development of Maxilla.)
4. Bulldog face: short maxillae (نمر) + Frontal bossing of skull.
5. Rhagades: linear scars at angles of Mouth.
6. Hutchinson teeth: (improper teeth development) Teeth CHARACTERISTICALLY:
   - Widely spaced
   - Shorter than Lat. Incisors
   - Thick in ant. post. diameters
   - Screw driver appearance: (deficient enamel) — Cutting ends narrow than the gingival ends.
   - Notched (d.t effect of Trauma)
7. Moon's Molars (Mulberry Molars): usually at 1st lower Molar; (1.4 cusps) are packed Together in The Center Instead of being at Corners → Dome shaped teeth with wider gingival Margin Than The Cutting ends.
8. onychia.

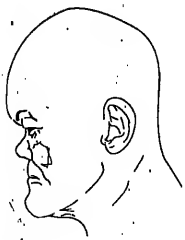
Stigmata of Late lesions (C) (appear)

(Ghost of I.K. Following stroke)

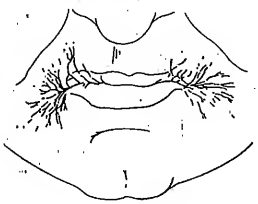
- Corneal Opacity d.t (IK)
- Optic atrophy
- Perceptive deafness (8th Nerve)
- Sabre tibia (Bowing of ant. Tibia)
- Frontal bossing of Skull (olympian Brow)
- perforating nasal Septum or Soft palat.

+ Hutchinson Triad (Triad of Syphilis)

CHARACTERISTICALLY of:
- Perceptive deafness
- Hutchinson Teeth
- IK



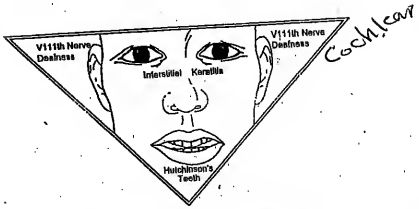
Bulldog face with saddle nose and relative prominence of lower jaw in late congenital $



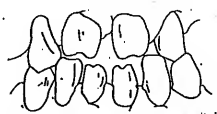
Scars at angles of mouth (rhagades) are stigmata of congenital syphilis

Gummatous destruction of the nasal septum and collapsed lower part of nose in late congenital $

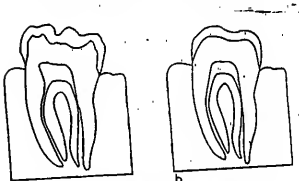
Clinical appearance of sabre tibia in late congenital $



Hutchinson's triad in late congenital $



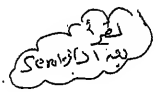
Hutchinson's incisors in late congenital $



Moon's molars in late congenital syphilis
(a) normal (b) abnormal

Diagnosis of Cong. S

1. CIP & Stigmata
2. Radiological Bone Exam.
3. DGM : From ← MM lesions, umbilical vein, Nasal secretions.
4. Serological testing (see profeta law):



if false +ve

↓

عشان نفرق بين الحقيقية :

(سؤال امتحان) either (1) Rising titer (VDRL)

(2) FTA-ABS test : using Fluorescein labelled IgM Conjugate. (Not The usuall Fluorescein labelled Antihuman globulin)

(IgM type).

↓

. Because IgM Can't Cross the placenta So diagnostic of +ve in fetus.

↓

But False -ve results may occur if "spill over" IgM From The mother occurs d.t. placental degeneration

Neonatal pustular eruptions*

1. Infantile acne.
2. Impetigo.
3. Congenital S.
4. Neonatal listeriosis.
5. HS.
6. Neonatal candidiasis (1)
7. Malassezia furfur.
8. Scabies.
9. Miliaria.
10. Eosinophilic pustulosis.
11. Toxic erythema neonatorum (2)
12. Infantile acropustulosis.
13. Transient neonatal pustulosis (3)
14. Pustular psoriasis (4)

* see also chapter 21, p. 108.

→ Asses Ceruloplasmin level.

. In Pregnant → double level of Non Pregnant Adult.

. In Infants → half of NL Adult.

So : Compare 2 Concentrations to detect if leakage have occured or not (leakage of IgM From mother to Fetus)

✓

ال rising titre ل VDRL

Serological Tests For Syphilis

Non specific Tests (non Treponemal tests or Reagin tests)

- simple - cheap - good - ve - follow up
- weather man

① VDRL (Venereal dis. Research Laboratory test)

② RPR

③ Automated reagin Tests (ART).

* These tests are non specific
  a. they depend on the use of an antigen other than T-Pallidum
- Thus Antigen Called: "Cardiolipin" is in alcoholic extract of beef heart muscle & has the ability to react with a specific gamma globulin present in the patient's serum Called "Reagin"

(Ag: Cardiolipin + Ab: Reagin) → Visible Reaction

- the regin: is present in Very small amount in all NL sera but in large amounts in Sera of Syphilitic patients. to the degree that when react with the cardiolipin can produce visible reaction either through flocculation or Complement fixation.

Flocculation tests

CFT (CWR)

Specific Tests (Treponemal tests)

- very costly
- sim.

- TPHA
- TPI Treponemal P. immobilization test
- FTA Fluorescent Treponemal Ab test (Fluorescent for 2)
- FTA Abs.
- RP-CFT (non pathogenic Treponema → Reiter protein - complement test)

these tests are specific as they depend on detection of treponemal Antigens. So named (Treponemal tests).

- Adv. they are accurate & don't give false results So used as Confirmatory For non specific tests.
- Disadv:
  1. expensive
  2. Technically difficult
  3. Remains +ve for life, So can't be used For follow up of the Results.

TPHA: TP Ag + rabbit RBCs + patient serum → TP

- not turn -ve → once +ve → +ve forever

Non Specific Tests

- Advantages: (1) easy (2) Cheap (3) Sensitive (So screening ; good -ve Tests). (4) Can be used to follow up the ttt results as they are become -ve (so effective ttt) Specially if quantitative estimation of their titer is used (Serial quantitative VDRL)

Used For:
- Screening (Sensitive - Good -ve)
- Follow up of ttt results

- Disadv. they may be false +ve or false -ve (so (non specific)) should be confirmed with one of the specific tests.

VDRL

False +ve

1. Technical faults
2. Pregnancy
3. Old age → Biological False +ve
4. Idiopathic (Variation in NL)
5. BFP: Conditions cause by Liberation of large amounts of Cardiolipin from organisms other than Treponema or d.t Cellular destruction as:
   - (a) Viral Pneumonia
   - (b) Malaria ✓
   - (c) Hepatitis. *
   - (d) Measles, Mumps.
   - (e) Chicken pox.
   - (f) Vaccinat°.
   - (g) Treponema (dis.) other than ♂

No anti Ab against T.P

(Vir. infn)

I. Acute Conditions (reaction +Ve For ≤ 6ms)

II. Chronic Conditions (reaction remains +Ve > 6ms)
   - (a) SLE
   - (b) Rheid
   - (c) Anemia
   - (d) leprosy (LL > TL)
   - (e) Mg
   - (f) Sarcoidosis
   - Dermatomyositis

if reactive False +ve → titre ↓↓

False -ve (d.t)

1. Prozone phenomenon

Failure of occurance of Flocculation reaction d.t high conc. of Abs in Patients Serum except after Serial dilution.

(only with Flocculation tests Not with CFT)

2. Mg ♂
3. HIV

→ Biological False +Ve Reaction (BFP)

(dog) patient é No Hx or clinical data of ♂ with
- +ve: non specific Tests
- -ve: Specific Tests.

AET
- Acute (For ≤ 6ms): Inf. / Immuni- Za tn
- Chr. (For > 6ms): leprosy / autoimmune SLE & RA

- Flocculation tests: < VDRL / RPR → Cardiolipin Ag + Small amount of pt. serum → Flocculation that can be detected by NE or Mic.

VDRL
RPR

« المستخدم هو VDRL »

- CFT (WR) (لا يستخدم):
  Cardiolipin + Serum (Reagin) + C. Addition → mix → add sensitized sheep RBCs (RBCs coated ē Anti RBCs) → Ab متضاد
  - if (-ve) hemolysis → (+ve) test (✓)
  - if (+ve) Hemolysis → (-ve) test (Not ✓).

- ART: VDRL ē auto-analyzer to perform Ag. How ??

Specific tests (Trep. المستخدم حالياً في مصر) (other Virulent Strains)

① TPHA: 2 tubes.

Test tube
↓
Sensitized sheep RBCs (Treponema Coated sheep RBCs)
+
pt. Serum.

Control tube
Non sensitized sheep RBCs
+
Patient Serum.

Test is +ve if there is agglutination in (test) tube "only".

أشهر اختبار .. وهو المستخدم حالياً في مصر.

② TPI : . Serum + Treponema + "C" Addition

DGM / Exam. → Immobilizat^ of Treponema.

. disadv. ① difficult
② delayed Result till end of 1st Year.

③ FTA test : Serum + Treponemae (dead) → Treponemal Coating by

Abs : to detect this Coating add "Conjugate" [Fluorscein labelled Anti human Igs] → Fluorscein under MiC.

④ FTAA test : as FTA but before doing it, the Serum is diluted (by) Culture extract of other Treponemae to Absorb non specific Abs. against Other Treponemas → So no false +Ve Results

"Reiter"

Adv ① No false +Ve results.
② the only test that +Ve in early Phase of Ig $\not\delta$. (2nd w)
③ used to $\not\varnothing$ Cong. $\not\delta$ More specifically "only"

If very early IH (revert to -Ve)

2 Standard tests For $\not\varnothing$ of Cong $\not\delta$.

• because : this test can be done by using specific class ($\not\delta$ Conjugate (IgM), Since IgM don't cross the placenta, a reactive test in infant specifically indicates Cong. $\not\delta$
However : frequent determination of Rising titer of VDRL is more easy & cheap (because FTAA sensetivity is < 90% in 1st month ↑ 60% after is ") so VDR Better

⑤ Reiter protein CFT: the Ag is protein derived from Reiter strain of Treponema That is antigenically similar to T. pallidum + Patient serum in presence of Complement

(Not used)

NB: on Serological Tests

... [A] onset of positivity.
[B] duration of "
[C] % of positivity in each stage.

[A] onset of positivity:

- FTAA (IgM) → end of 2nd W.
- FTAA (ordinary) → during 3rd W.
- TPHA → " " "
- Non specific tests → 3-4 wks after Inf. (1-2 Ws after appearance of Chancre)
- TPI : → after end of 2ry stage (>12 Ws)

FTAA (IgM) → FTAA (ordinary) → TPHA → Non Specific Tests (VDRL) → TPI

Use:
① Neonatal & (But False +Ve (10%) : in placental degeneration ; False -Ve (30%) : after 1st m.; ↓ sensitivity) So Quantitative VDRL done
② very Early Diagnosis of Chancre (when IGM is -Ve)
③ ± Follow

So it's the Most Sensitive in 1ry Stage.

[B] Duration of positivity: see below.

سؤال جامد

How long do serological tests For ♀ remain +ve ??

A. Non specific serological tests → All remains +ve Except after ttt.

If ttt started ...
- Before +ve tests (<3-4ws) → No sero +ve & pt. remains sero-Ve
- after +ve tests (in 1ry & 2ry stages) → sero-ve after 3-5 m- From Initiation of ttt
- In Latent & Late ♀: progressive slow ↓ in sero +ve till become sero (-Ve)

Except: Some cases remains with Fixed titer (Sero fast or W.R Fast)

B Specific serological tests: all remains +ve For life (Even ē ttt). Except FTAA (IgM) ↓↓ ēin months (Specially ē ttt)

↘ (So this) the only specific tool That can be used to Follow up ♀ ttt

يعني جامعة

- Non specific tests: Their Titer ↓ with ttt EXCEPT Sero fast condition
- Specific tests: once ve, always +ve Except FTAA (IgM)

(قاعدتين كل واحدة فيها استثناء)

C- ♀ positivity:

- 1ry stage → 50% +ve
- 2ry " → 100% +ve (Except ♀)
- late ♀ → Most +ve ē Except ♀ FTAA (IgM).

Treatment of S

- Basic principles:

1. Penicillin G → ## of Choice
2. Treponema multiply 1 30 hrs & this requires Treponemicidal level in tissues for at least 8 ds.
3. Any organ can be affected by T. pallidum including the brain & this require drug That can cross the BBB.

So Procaine penicillin & Crystalline P.

أفضل من → Benzathine Penicillin. (as they can cross BBB).
(Lipid insoluble. Can't pass BBB).

IVB. Types of penicillin:

1. Crystalline Penicillin (1 million U/ ampoule) < IM or IV
2. Procaine Penicillin (600000 U/amp.) → IM only
3. Benzathine Penicillin (1.2 MU/amp) → IM only
   ↓ don't pass BBB

"طويل المفعول"

Note: "بشتغل"
- Benzathin P → "Compliance" أفضل شيء
- Procain & Crystallin P. → (BBB) أفضل شيء
  use for Neuro S

Treatment

① Probenecid (بروبنسيد) — except Neuro
② Cs

Early S (< 2 yrs)

① Procaine P: (أمبول عضل يوميا لمدة ١٠ أيام) 600,000
② Benzathine P: (أمبول واحد عضل) 50,000 U/kg

Late S (> 2 yrs) (Gumma & CV S)

① Procaine P
② Benzathine P.

= (أمبول عضل يوميا لمدة ١٠ أيام) أو (أمبول عضل كل أسبوع لمدة ٣ أسابيع)

(A) Neuro S & ocular S → (1) علاج لمدة ١٠ أيام من

- Crystalline P (أمبول كل ٤ ساعات)
- أو
- Procaine P (٤ أمبول عضل يوميا)

(2) Amoxycillin [6 gm/d for 20 ds.] (Adl pr. Penicid)

(3) Ceftriaxone: 2gm IM or IV for 20 ds. daily.

NB
- in All Penicillin ## Cases: give 1 gm of probenecid 1 day before penicillin Inj.
- Why?
  1. ↓ renal Exc. → ↑ level of P
  2. displacement of P from plasma protein → ↑ level
- Except in ## of Neuro S
- why
  1. may ## with Pn distribution of P. in brain
  2. ↑ Adverse Reac.

Neonatal Syphilis: Neonate with:

Proven or highly probable or has mother with untreated Early S (لم تعالج أثناء الحمل)

- Procaine 50,000 U/kg/d IM x 10 ds
- Crystalline (IV) < 7 ds: 50,000 U/kg x 2/d IV; 3 ds: 〃 x 3/d IV [100–150,000 U/kg/d IV]

No signs of dis. or born to mother Treated S → Benzathine 50,000 U/kg (طويل المفعول حبة واحدة) (Benzath.)

Treatment in other Situations:

(1) Pregnant: as in non pregnant Adult

if there is penicillin Allergy → Azithromycin ; Erythromycin ; Ceftriaxone

- VDRL: done quantitively three delivery to detect any Clinical or serological relapse.

No tetracychline

(2) The following treated as Neuro S: < ocular / HIV

a. HIV (.. See) (d.t High Incid. ♀ Neuro S)

b. Optic atrophy or Nerve deafness (Add: Cs)

c. (IK) ? (add 0.5 prednisolone EDs or Atropine EDs. ↓ Eye drop.)

جيا "Amoxycillin"

(3) In Cases of penicillin allergy:

- Tetracycline Hcl. 2gm daily
- Doxycline: 200 mg "
- Erythromycin: 2gm daily

for: 15ds: in Early stage

30ds: Late stage

NB: Azithromycin may be used:

- Early S → 2gm Single dose.
- pregnant → [illegible] (1g)

- Ceftriaxone:

also pregnant → Early S → 1gm Id for 1 w.

Neuro S → 2gm Id " 20ds

لو حامل ... ممكن يستعملين

- Tetra, Doxy, Cotrim. (15ds / 30ds)
- Erythro, AZythro, Ciprofloxacin
- Amox. Coll.

- Follow up of ♂ Patient: By (VDRL):

  1. 1, 3, 6, 12 months after Tt
     For < upto 2 yrs: in Early ♂
     < upto 3 yrs: in Late ♂

  2. Neuro ♂ or AbNL CSF: CSF exam / 6 months
     Tt'p < NL Cell counts
     −Ve CSF VDRL.

- Re Treatment if.:

  ① Clinical relapse → persistent or recurrent S & S

  ② Serological → Sustained 4 Fold ↑ in VDRL
  Failed ↓ in VDRL < 4 Fold
  even 1 yr after Tt
  (treat as late ♂)

Reaction to Tt

① Penicillin Reactions:

ⓐ Immediate < Urticaria, Angioedema, Anaphylactic shock. } → Tt: lie down & Feet raised. air way; adrenaline 1/1000 0.5–1 ml (IM); Hydrocortisone 250 mg (IM); Aminophylline 250 mg IM

ⓑ delayed: 1–2 wks. CIP < Serum sickness like; skin rash; Fever, arthralgia, proteinuria & EN

Tt: antihistamines.

② Procaine Reaction: (Hoigne's reaction):

d.t Procaine Fract (occur & < Benzathine & Amoxycillin.)

Acute Non Allergic Psychiatric Reacts

- Tachycardia
- Cyanosis
- Confusion
- Hallucinations

Tt: No Tt, Spent ↓↓ even in 1 hr.

③ Jarish - Herxheimer Reaction: ✗ (اختياري)

AET: Allergic reaction (Not drug reaction)
That occurs with the First dose of Anti Syphilitic ## (Penicillin).

Fillor add or None Rule: يعطى كل أو لا يعطى (لا يعطى جزئياً)

. Mech. anti ✗ ## may → ① released Treponemal endotoxins
or ② Antibodies formation after rapid release of Treponemal Ags.

. onset: 3-12 hours after 1st injected dose.

. CIP

Early ✗ (More common)
affect 50% of pts.
. usually: Mild
. CIP ① FAHM
② Inflamm. of Pre-existing ✗ lesions:
. Chancre
. L.N
. Skin Rash

Late ✗ (More dangerous)
. affect 25% of pts.
. may be mild (Fever) or dangerous
① in ✗ Aortitis → Coronary occlusion
② in ✗ Laryngitis → suffocal.
③ GPI → Convulsion

(ع مرض بوبا)
. مرض هوستاكريشيم يوم قبل البدء
وطفح يوميين بعد العلاج يكتب صريحا

. ## ① Prevention
② Active ## → Cs

④ Therapeutic paradox: worsening of the dis. after ## d.t Excessive scarring produced by too rapid destruction of Treponemas

. More in patients with Aortic dis

⑤ Vaso vagal attack: lying down & elevated legs.

HIV & S:

. S & other STDs that produce genital ulcers further ↑ risk of HIV Acquiring d.t

① Lack of epithelial barier d.t ulcerat

② large No of Macrophages & CD4 that Expres HIV receptors.

③ Treponema ++ Macrophages → Cytokines.

S. In HIV Patient ch By

① ↑ Incid of ulceration in 2ry lesson.

② ↑ Incid. of Bact. effect of Chancre →

③ ↑ " " Neuro S. Painful chanc

④ Serology may be { Very high / Low / Non Reactive } (5) Ø

Done BY Biopsy.

⑤ HI → ↑

Treat as Neuro S

. + CSF → Treat as Neur

. - CSF → " as Late

SEXUALLY TRANSMITTED AND TRANSMISSIBLE PATHOGENS	
Bacteria	*Neisseria gonorrhoeae* *Treponema pallidum* *Haemophilus ducreyi* *Chlamydia trachomatis* *Mycoplasma hominis, M. genitalium* *Ureaplasma urealyticum* *Gardnerella vaginalis* *Mobiluncus curtisii, M. mulieris* *Calymmatobacterium (Klebsiella) granulomatis* *Shigella* spp. *Campylobacter* spp. *Helicobacter cinaedi, H. fennelliae*
Viruses	Human immunodeficiency virus, types 1 and 2 Herpes simplex virus, types 2 > 1 Human papillomavirus Hepatitis viruses, B > C and (via fecal-oral contact) A Cytomegalovirus Molluscum contagiosum virus Human T-cell lymphotrophic virus, types I and II Human herpes virus, type 8
Protozoa	*Trichomonas vaginalis* *Entamoeba histolytica* *Giardia lamblia*
Fungi	*Candida albicans*
Ectoparasites	*Phthirus pubis* *Sarcoptes scabiei*

Table 31.1 Sexually transmitted and transmissible pathogens.